LAPAROSCOPIC AND OPEN SURGICAL STAGING FOR ADENOCARCINOMA OF THE ENDOMETRIUM – AN ANALYSIS

This dissertation is submitted to

THE TAMILNADU

Dr. MGR MEDICAL UNIVERSITY

in partial fulfillment of the requirements for the award of degree of

MCh (BRANCH VII)

SURGICAL ONCOLOGY

COLLEGE OF ONCOLOGICAL SCIENCES

CANCER INSTITUTE (WIA)

ADYAR

CHENNAI – 600 020

AUGUST 2012

CERTIFICATE

I hereby certify that this dissertation on **"Laparoscopic and Open Surgical Staging for Adenocarcinoma of the Endometrium – an Analysis"** is a bona fide work done by **DR.R.BALAJI**, in the department of Surgical Oncology, College of Oncological sciences, Cancer Institute (WIA), Chennai, under my guidance and supervision, to my satisfaction.

Prof. E.HEMANTH RAJ MS, M Ch, PhD

Additional Director and Chairman

Division of Surgical Oncology

Cancer Institute (WIA)

Adyar, Chennai – 36.

ACKNOWLEDGEMENT

I express my sincere thanks and deepest sense of gratitude to our Professor and Chairman, Division of Surgical Oncology, **Dr E Hemanth Raj** M Ch PhD**,** for his scholarly guidance, masterly supervision, and encouragement in completing this project.

I humbly record my deep sense of gratitude to **Dr. Sridevi** M Ch, Professor, Division of surgical oncology, for her constant support, encouragement and guidance during the course of this study.

Words are few to express the gratitude and the inspiration I have drawn from the leaders in the realm of oncology in India, **Dr. Krishnamurthy**, Advisor and **Dr. V Shantha**, Executive Chairman, Cancer Institute (WIA).

The task would have been indeed more difficult without the help of Mr. Rajagopal and Mr.Sivakumar and the other staff of Tumor Registry at Cancer Institute (WIA), who had the unenviable task of procuring all the case records instantaneously on demand.

Last but not the least; I thank all my patients for their kind co-operation in this study.

CONTENTS

AIM OF THE STUDY

Primary Objective:

1. To compare the patient, surgical, pathological and treatment characteristics of open and laparoscopic surgical staging for adenocarcinoma of the endometrium
2. To analyse the factors affecting the above outcomes after laparoscopic and open surgical staging for adenocarcinoma of the endometrium

Secondary Objective:

To determine the Disease Free Survival (DFS) and Overall Survival (OS) after open and laparoscopic surgical staging for adenocarcinoma of the endometrium

BACKGROUND

The management of gynaecological malignancies forms a major part of any surgical oncologist's practise. Endometrial adenocarcinoma ranks third among gynaecological malignancies after cervix and ovarian cancer according to the MMTR database. The incidence of endometrial adenocarcinoma is about 2.8/100000 population. (1) This is in contrast to the US population where it ranks first among the gynaecological malignancies is the fourth most common cancer in females after breast, lung and colorectal cancers. (2)

Two different clinicopathological subtypes of endometrial cancer are recognized: the estrogen-related (type I,endometrioid), and the non-estrogen-related (type II, nonendometrioid). Endometrioid tumours show microsatellite instability and mutations in PTEN, PIK3CA, K-ras, and CTNNBI (β-catenin), while nonendometrioid (predominantly serous and clear cell) tumours exhibit p53 mutations and chromosomal instability (3).

The average age of patients with endometrioid cancer is approximately 63 years, and about 70% are confined to the corpus at the time of diagnosis and they have a 5-year survival of approximately 83% . In contrast, the average age of patients with nonendometrioid cancer is 67 years, and more than 50% have already spread beyond the corpus at the time of diagnosis. They have a 5-year survival is approximately 62% for clear cell carcinomas and 53% for papillary serous cancers (4).

Most patients with endometrial adenocarcinoma present with postmenopausal bleeding. The diagnosis should also be considered in patients with postmenopausal

presentation of pyometra, peri-menopausal women with heavy inter-menstrual bleed or presence of atypical endometrial cells on Pap smear. Endometrial cancer accounts for about 15% of all patients who present with postmenopausal bleeding. (5) All patients suspected of having endometrial carcinoma should have endocervical curettage and endometrial biopsy. A histologically positive endometrial biopsy allows the planning of definitive treatment.

Because there is a false negative rate of approximately 10%, a negative endometrial biopsy in a symptomatic patient must be followed by a fractional curettage under anesthesia. A diagnosis of endometrial hyperplasia on endometrial biopsy does not obviate the need for further investigation.

Fractional curettage entails bimanual recto-vaginal examination under anesthesia, curettage of the endocervical canal, cervical dilatation and systematic endometrial curettage. The tissues are placed in a separate container so that the histopathologic status of the endocervix and endometrium can be determined separately.

Routine preoperative investigations for early stage endometrial carcinoma include a renal (RFT) and liver function tests(LFT) and a complete hemogram. A pelvic and abdominal computed tomographic (CT) scan may be helpful to determine the extent of metastatic disease in patients where distant metastases are suspected due to the presence of clinical hepatomegaly, altered LFT, palpable abdominal mass or pelvic disease , ascitis and high risk histologies. However CT cannot help differentiate the depth of myometrial invasion in which MRI scores over CT.

The staging of endometrial adenocarcinoma is done according to the 2008 FIGO staging which is a surgico-pathological staging system. (6) The 1971 FIGO Staging was a clinical one followed by its revision in 1988 which made it a surgico-pathological staging and the subsequent revision has come in 2008 with alteration in stage mainly excluding cervical glandular involvement alone and peritoneal cytology as prognostic factors and differentiating subgroups of pelvic and para aortic nodal involvement.

The foundation of management of endometrial carcinoma is surgery which entails a Total abdominal hysterectomy (TAH) with Bilateral salphingo oophrectomy (BSO). Extended surgical staging (7) in the form of peritoneal biopsies, omentectomy and pelvic and para aortic nodal lymphadenectomy is needed in patients with high-risk disease (grade 3, serous or clear cell histologies, stages IC or II disease). This has been traditionally achieved by a laparotomy but with the advent of laparoscopy as a surgical tool, it has found application in the management of various malignancies and has made major strides in the surgical management of endometrial carcinoma also.

The use of laparoscopy for staging has reduced hospital stay& long term hospital costs and facilitated earlier return to normal activity with equivalent oncologic outcomes. The pitfalls of operating laparoscopically on obese patients and the issue of nodal yield have been found to be improved with increasing experience of the operating surgeon.

There are few studies on the laparoscopic surgical staging of endometrial carcinoma in our country and hence we analysed patients who had been treated by this method in our Institute and compared them with patients who underwent open surgical staging to evaluate for complications and outcomes in the setting of a tertiary cancer care centre.

MATERIALS AND METHODS

A retrospective analysis of all patients who presented with adenocarcinoma of the endometrium and treated surgically at the Cancer Institute (WIA) from the year 2006 to 2010 was done. A total of 145 patients with adenocarcinoma of the endometrium that underwent surgical staging by open or laparoscopic method were analysed. Thirty five patients with histologies other than adenocarcinoma like squamous cell carcinoma and carcino-sarcomas and those with endocervical adenocarcinomas were excluded from the study.

All patients had a biopsy done by dilatation & curettage to establish a histological diagnosis. In some patients the diagnosis was established intra-operatively by frozen section study and then surgical staging was done. Pre-treatment evaluation was done by a thorough history, physical examination, basic investigations, ultrasound of the abdomen and pelvis and a chest X-ray and where necessary a CT scan of abdomen and pelvis.

Each patient was evaluated by a multidisciplinary team before therapy was initiated. The clinical team included a surgical and radiation oncologist with help from our experienced medical oncologists, radiologists and pathologists as and when required.

After obtaining an informed consent, treatment was initiated. Patients with high grade tumours were treated with one or two fractions of High Dose Rate (HDR) Intra Cavitary Application (ICA) brachytherapy. (Heyman et al (8), Sause et al (9), Weigenserg et al (10))

Subsequently they underwent surgical staging two to five days after brachytherapy. Surgical staging included peritoneal wash cytology, total abdominal hysterectomy, bilateral salphingo oophrectomy, omental and peritoneal biopsies and bilateral pelvic lymph node dissection. Pelvic lymph node dissection was done from above the level of bifurcation of the common iliac vessels superiorly, to the circumflex iliac vein inferiorly, genito-femoral nerve laterally and the bladder medially. This dissection encompassed nodes over the common iliac, internal and external iliac vessels, and hypogastric and obturator nodes. We did not dissect the para aortic nodes unless they were grossly enlarged or unless there was gross pelvic nodal involvement as the *therapeutic role* of para aortic nodal dissection is still a matter of controversy.

For the laparoscopic approach five port technique with bilateral para-rectal ports and iliac ports and supra-umbilical camera port. The diagnostic laparoscopy is done first along with peritoneal fluid cytology followed by the rest of surgical staging as described previously.

After surgery, all patients with high risk factors for recurrence like grade 3 tumour, non-endometroid histology, deep myometrial invasion (greater than half of myometrium), nodal involvement or cervical involvement by tumour were treated with adjuvant radiation. The adjuvant radiation was in the form of external beam pelvic radiation to a total dose of 50 Gy with a concomitant vaginal boost of 6 to 8 Gy for some patients and addition of para aortic nodal radiation to a dose of 40-41 Gy in patients with multiple positive pelvic nodes.

The pelvic radiation was delivered through a CRT (Conformal Radio Therapy) Technique by five field method (2 pairs of lateral oblique fields and one anterior field). The vaginal boost was delivered by HDR ICA brachytherapy to deliver 600-850 cGy to vaginal mucosa. Para aortic nodal radiation was delivered by a field the upper border from T12 L1 junction to the lower border concordant with the pelvic field at about the level of L5 S1. Patients with multiple positive para aortic or pelvic nodes or peritoneal involvement received adjuvant taxane and platin based chemotherapy.

The patients were kept on regular follow up by three-monthly clinical examination for the first three years, six monthly visits for the fourth and fifth year and annually thereafter. Annual ultrasound of the abdomen and pelvis and chest X-ray were also done.

The data collected from the case records were analysed using SPSS for Windows version 17.

1. **Patient characters** like age, co-morbid illnesses and BMI,
2. **Surgical parameters** like operating time, blood loss, duration of hospital stay and post- operative complications,
3. **Pathological characters** like nodal yield, pre operative and post-operative tumour grade, FIGO stage, uterus and tumour size and
4. **Treatment parameters** like use of pre-operative ICA, adjuvant radiation, and adjuvant chemotherapy were analysed in the laparoscopic and open surgical staging groups.

Pearson's Chi-square test by cross table and independent sample T-test were used for univariate analysis while Binary Logistic Regression was used for Multivariate analysis. Survival analysis was done by the life table method and Kaplan Meir plots.

REVIEW OF LITERATURE

Endometrial adenocarcinoma is the third most common gynaecological malignancy after cervix and ovarian carcinomas. In Chennai, the Crude Incidence Rate (CIR) of uterine corpus malignancies is 2.8/100,000 according to the MMTR database. It has shown a steady increase in Age Standardized Rate (ASR) from 1.6 in 1993 to the current ASR of 3.1 with an average annual change of 3.7%. Corpus uterine cancers accounted for 3% of all cancers in females. The cumulative lifetime risk of developing corpus uterine cancers was 1 in 249(0-74 years). (1)

Epidemiologic Risk Factors for Endometrial Carcinoma (7)

Factors	***Relative Risk***
Chronic estrogenic stimulation	
Estrogen replacement (no progestin)	2-12
Obesity	10
Early menarche/late menopause	1.6-4.0
Nulliparity	2-3

Demographic characteristics

Increasing age	4 – 8
White race	2
High socioeconomic status	1.3
European/North American country	2 – 3
Family history of endometrial cancer	2

Associated medical illness

Diabetes mellitus	3
Gallbladder disease	3.7
Hypertension	1.5
Prior pelvic radiotherapy	8

Patterns of Spread:

Spread of Endometrial carcinoma occurs by the following routes

- direct extension to adjacent structures
- transtubal passage of shed tumour cells
- lymphatic dissemination
- hematogenous dissemination
- Endocervical and trans-cervical extension

Prognostic Variables

Though the stage of disease at presentation is the most important prognostic variable in endometrial carcinoma there are other factors that have an impact on disease recurrence and survival.

Some of these are

1. Age – Greater than 40 years (11)
2. Histological subtype – non endometroid type (12,13,14,15)
3. Myometrial invasion – outer half (16)
4. Vascular invasion – increased recurrence and death in stage I (17)
5. Peritoneal cytology results – Possibly dependent on other variables (18)
6. Hormone receptor status – better prognosis even in node positive disease (19)
7. Nuclear grade – better prognostication than tumour grade (20)
8. DNA ploidy – Stronger prognostic factor than age and grade (21)
9. Tumour size – prognostic cut-off at 2 cm (22)

Treatment of Endometrial Cancer

The management of endometrial cancer has changed significantly over the last 40 to 50 years. In the 1970s era, endometrial cancer was clinically staged using the 1971 clinical FIGO staging where Stage IA was uterine corpus confined cancers – uterine cavity length <=8cm; Stage IB was uterine corpus confined cancers – uterine cavity length >8cm; Stage II was cancers with cervical involvement; Stage III was cancers with

extra-uterine spread but still confined to the pelvis and Stage IV was cancers with adjacent organ invasion or distant metastases. Patients with early-stage disease were treated with preoperative packing of the endometrial cavity with radiation sources, Heyman's capsules followed by hysterectomy. (8)

The International Federation of Gynecology and Obstetrics (FIGO) approved a surgical staging system for endometrial cancer in its revision of staging in 1988. (23) This acknowledged the shift to surgery as primary therapy, with pelvic radiotherapy being used postoperatively as adjuvant therapy for women at increased risk for recurrence.

The latest revision of the FIGO staging published in 2009 made the following changes

1. Stage I had only two subgroups - <=1/2 and >1/2 myometrial invasion
2. Cervical glandular invasion was removed and only stromal invasion was taken into consideration and made as Stage II
3. The involvement of nodes were sub-classified into two groups as Stage IIIC1(pelvic nodes) and Stage IIIC2(Para aortic nodes)
4. Peritoneal cytology was disregarded in the stage grouping

Revised FIGO staging for carcinoma of the endometrium. (6)			
Stage I*			**Tumour confined to the corpus uteri**
	IA*		**No or less than half myometrial invasion**
	IB*		**Invasion equal to or more than half of the myometrium**
Stage II*			**Tumour invades cervical stroma, but does not extend beyond the uterus****
Stage III*			**Local and/or regional spread of the tumour**
	IIIA*		**Tumour invades the serosa of the corpus uteri and/or adnexae#**
	IIIB*		**Vaginal and/or parametrial involvement#**
	IIIC*		**Metastases to pelvic and/or para aortic lymph nodes#**
		IIIC1*	**Positive pelvic nodes**
		IIIC2*	**Positive para aortic lymph nodes with or without positive pelvic lymph nodes**
Stage IV*			**Tumour invades bladder and/or bowel mucosa, and/or distant metastases**

	IVA*		**Tumour invasion of bladder and/or bowel mucosa**
	IVB*		**Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes**

***Either G1, G2, or G3. ** Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.**

 # Positive cytology has to be reported separately without changing the stage.

The traditional approach for the treatment of endometrial cancer by laparotomy is increasingly being replaced by laparoscopic surgery. Like laparotomy, operative laparoscopy can accomplish the full surgical procedure, which includes doing a complete intra-peritoneal survey, obtaining peritoneal washings, removing of the adnexae and performing pelvic and para aortic lymphadenectomy and total hysterectomy. The advantages of laparoscopy are well-documented. Laparoscopy avoids the morbidity of a laparotomy, overcomes the limitations of vaginal hysterectomy, provides adequate histo-pathological information for accurate surgical staging and hastens the postoperative recovery of patients.

The performance of a pelvic and para aortic lymphadenectomy is the key procedure for the staging of this cancer. In 1989, Dargent and Salvat (24) from France used the laparoscope to perform limited pelvic lymphadenectomy in women with cervical

cancer. In 1991, Childers and Surwit (25) published their report on pelvic and para aortic lymphadenectomy performed along with a laparoscopic assisted vaginal hysterectomy (LAVH) and bilateral salphingo-oophorectomy (BSO) in two women with endometrial cancer.

Childers et al. (26) reported their series of 59 patients with endometrial cancer who were staged laparoscopically combined with a vaginal hysterectomy and bilateral salphingo-oophorectomy. Among them thirty- one patients were deemed candidates for staging based on criteria like high-grade or deep myometrial invasion and lymph node dissection was completed in 29 patients (obesity precluded it in two patients), with a feasibility rate of 93%. There were three major and three minor complications. The average hospital stay was 2.9 days, but there was no data on operative time, lymph nodal yield, and cost analysis. These early series emphasized pelvic lymphadenectomy, but it remained necessary to do laparoscopic para aortic lymphadenectomy for laparoscopy to be fully accepted as a technique to stage endometrial cancers.

Childers et al. (27) published their experience in para aortic lymphadenectomy extending from the duodenum to the bifurcation in 61 patients with cervical, endometrial, or ovarian cancer in 1993. Obesity prevented the completion of the surgery in three patients (5%) and in one patient (0.8%), conversion was needed in view of extensive adhesions.

Data on lymph node yield were available in 23 patients. For the right-sided dissection, there was an average nodal yield of three. The operating time for lymphadenectomy for the six patients who underwent para aortic lymphadenectomy

ranged from 25 to 70 minutes, depending on the unilateral or bilateral nature of procedure. The hospital stay for the 33 patients undergoing laparoscopic lymphadenectomy was 1.3 days. There was one vena caval injury that required transfusion and laparotomy, a complication rate comparable with that of open surgery. Two patients had complications related to the hysterectomy: One had a transected ureter caused by the endoscopic stapler, and one had a cystotomy.

In 1995, Spirtos et al. (28) reported on 40 patients who underwent bilateral partial para aortic nodal sampling. There were five conversions to laparotomy in their study - two to remove unsuspected metastases, two for control of hemorrhage, and one because of equipment failure. The left-sided dissection was judged to be inadequate in two patients, which was an overall failure rate of 12.5%. On an average eight para aortic lymph nodes was removed: four from the right side and four from the left side. The mean operative time was 3 hours, 13 minutes, and the average hospital stay was 2.9 days.

In one of the largest series of laparoscopic lymphadenectomy, Koehler et al.(29) published their report on 650 patients undergoing laparoscopic transperitoneal pelvic (n = 499) or para aortic (n = 468) (combined pelvic and para aortic n = 362) lymphadenectomies. The mean number of pelvic lymph nodes removed from 1994 to 2003 remained fairly constant (16.9-21.9). On the contrary, the mean number of para aortic lymph nodes increased from 5.5 in 1994 to 18.5 in 2003, reflecting improvements in technique with increasing experience. The incidence of intra-operative complications (bowel or vessel injury) was 2.9% of patients while the incidence of postoperative complications was 5.8% with an overall complication rate of 8.7%. The authors reported

that no major intra-operative complications were encountered during the last five years of the study.

Similar results were reported by Querleu et al. (30) in their experience with transperitoneal and extraperitoneal lymph node dissections in 1,000 gynecologic cancer patients. There were 777 pelvic (757 transperitoneal, 20 extraperitoneal) and 415 aortic lymphadenectomies (155 transperitoneal, 260 extraperitoneal) in this study on patients with cervical, vaginal, endometrial and ovarian carcinoma. There were 182 patients with endometrial carcinoma. The average number of pelvic lymph nodes removed was 18 via a transperitoneal approach and the average number of para aortic lymph nodes removed was 17 via a transperitoneal approach versus 21 via an extraperitoneal approach. The authors reported an increase in the number of lymph nodes removed with increasing experience, yielding an average of 24 pelvic and 22 aortic lymph nodes in 2003. Intra-operative complications occurred in a total of 2% of patients including injury to vascular structures (1.1%); bowel (0.3%); ureter (0.3%); and nerves (0.3%). Five patients underwent conversion to laparotomy for completion of the lymph node dissection, secondary to fixed nodes or extensive adhesions. Conversion to laparotomy occurred in an additional two patients secondary to bowel or ureteric injury. Five patients required a second surgical intervention due to postoperative complications, most commonly bowel obstruction (n = 4).

These studies have demonstrated the ability of laparoscopic surgeons to perform pelvic and para aortic lymphadenectomy. The American Medical Association Physicians Current Procedure Terminology (CPT 2007) lists a total of four laparoscopic lymph node

dissection procedures, including total pelvic lymphadenectomy and para aortic lymph node sampling. Laparoscopic surgery has been used by many oncologic surgeons, and has been applied to nearly every disease site in gynecologic oncology.

Spirtos et al. (31) reported on 13 patients who underwent laparoscopic staging and hysterectomy as compared to 17 patients who underwent laparotomy. The laparotomy group required significantly longer hospitalization, (6.3 vs. 2.4 days, $p < 0.001$), took longer to return to normal activity (5.3 weeks vs. 2.4 weeks, $p < 0.0001$) and incurred higher overall hospital costs ($19,158 vs. $13,988, $p < 0.05$). The patients having laparotomy were significantly more obese and had a higher body mass index (BMI) (30.2 vs. 24.2).

The advantages with laparoscopic staging include significantly shorter post-operative stay, faster recovery and earlier return to activity coupled with lower overall cost. The longer operating time needed for laparoscopic staging is related to the experience of the surgeon as has been shown by Mendelez et al (32). In their study on laparoscopic staging for endometrial cancer, the operative time for staging decreased from a mean of 196 minutes for the first 25 patients to 128 minutes for the last 25 patients. Hospital stay decreased from 3.2 days to 1.8 days. The decrease in operative time with increasing experience and decreased hospital stay, coupled with the diminished use of expensive, disposable instruments, has led to a significant cost savings for laparoscopy.

One commonly quoted limitation of laparoscopic surgery is its use in patients with higher BMI as is the case with most patients with adenocarcinoma of the

endometrium who often have BMI greater than 35. As surgical skills have grown, laparoscopy has been used successfully in these women. Holub et al. (33) completed staging laparotomy for endometrial cancer successfully in 94.4% of 33 patients with BMIs of 30 to 40. Eltabbakh et al. (34) completed laparoscopic surgical staging in 88% of 42 women with BMIs of 28 to 60. In both studies, the benefits of shorter hospital stay with faster recovery were verified. However, many retrospective studies comparing laparoscopy and laparotomy have reported a significantly lower BMI in patients undergoing laparoscopic management, reflecting a selection bias favoring open procedures in obese patients.

Long-term survival and recurrence have been reported in several papers by Eltabbakh et al,(35) Malur S et al(36), Obermair et al (37) Zapico et al (38) and Kalogiannidis et al (39). In these series, more than 900 patients have been studied for a median of 16 to 53 months. The recurrence rate following laparoscopic management ranged from 0% to 9%. When compared to historical controls undergoing laparotomy and adjusting for factors such as stage, grade, age, and weight, there was no difference in survival in any of these studies.

In the study by Eltabbakh et al, (35) one hundred women had laparoscopic surgical staging and 86 underwent open surgical staging. There were no significant differences in the two groups in terms of patient factors like age, menopausal status, parity or tumour factors like histology, surgical stage, tumour grade or surgical factors like lymphadenectomy and use of postoperative radiation therapy. Women who underwent laparoscopic staging and those who had open surgical staging had 2-year and

5-year recurrence-free survival rates of 93% vs. 94% and 90% vs. 92%, respectively. There was a similar trend in 2-year overall survival (98% vs. 96%) and 5-year overall survival rates (92% vs. 92%, respectively). Between both groups, there was no difference with regard to the site of recurrence. By univariate and multivariate analyses, the approach used did not have any impact on survival. Only tumour grade, surgical stage, and histology were found to have a significant effect on survival.

In Germany, Malur et al. (36) prospectively compared thirty-three patients who were treated by conventional laparotomy to thirty-seven patients treated by a laparoscopic assisted vaginal approach. There was no significant difference between the two groups with regard to the number of lymph nodes, mean body mass index and mean operating time. The mean follow-up for the laparotomy group was 21.6 months compared to 16.5 months for the laparoscopy group. The recurrence-free survival rate was 97.3% for the laparoscopy group and 93.3% for laparotomy group and it was not statistically significant. Similarly, the overall survival rate was 90.9% in the laparotomy group and 83.9% in the laparoscopic group

Tozzi et al. (40) published the first report on survival out-comes in endometrial cancer from a randomized, prospective clinical trial analyzing laparotomy versus laparoscopy. With a median follow-up of 44 months, the authors reported that patients with stage I endometrial cancer had disease-free survival rates 93.8% (in the laparotomy group) and 91.2% (in the laparoscopic group). The overall survival rate was not statistically significant at 89.7% versus 86.3%, respectively.

The landmark prospective Randomized Control Trial comparing the laparoscopic and open surgical staging was the multi institutional GOG - LAP 2 trial by Walker et al. (41) The conversion rate was 25.8% (394 patients)(Due to bleeding in 49 patients (2.9%) poor visualisation in 246 patients (14.6%), metastatic disease in 69 patients (4.1%) and miscellaneous causes in 70 patients (4.2%)). Laparoscopy had fewer postoperative complications than laparotomy (14% v 21%, respectively; $P < 0.0001$) but similar rates of intra-operative complications. The median operative time was significantly in the laparoscopy group (204 v 130 minutes, $P < 0.001$). In the laparoscopy group the duration of hospital stay was significantly shorter (52% v 94%, respectively; $P <0.0001$). This study indicates that surgical staging for endometrial adenocarcinoma can be performed with laparoscopy with fewer postoperative complications, shorter hospital stay and without increased risk of intra-operative injuries.

The update to the study dealing with recurrence and survival was published online in January 2012. (42) There were 309 recurrences (210 in laparoscopy group; 99 in the laparotomy group) and 350 deaths (229 in the laparoscopy group; 121 in the laparotomy group) with a median follow-up of 59 months in 2,181 patients still alive. The hazard ratio for laparoscopy relative to laparotomy was 1.14 (90% lower limit, 0.92; 95% upper limit, 1.46), thus not meeting the definition of non-inferiority (falling short by 0.14) as specified in the protocol. However, the actual recurrence rates were substantially lower than anticipated, resulting in an estimated 3-year recurrence rate of 10.2% with open surgery group and 11.4% with laparoscopy group or a difference of 1.14% (90% lower limit, -1.28; 95% upper limit, 4.0). The 5-year overall survival was almost the same in both arms at 89.8%.

There are two meta-analyses that have compared the two techniques of surgical staging. In the analysis by Palomba et al. (43) four Randomised Control Trials (RCT) were identified and included for analysis. There was no significant difference in the laparoscopic and open approaches to endometrial cancer in disease-free survival (OR = 0.76, 95%CI 0.34 to 1.72, P = 0.655) overall survival [odds ratio (OR) = 0.80, 95%CI 0.37 to 1.70, P = 0.695] or cancer-related (OR = 0.89, 95%CI 0.19 to 4.13, P = 0.815) survival. The operative time was significantly longer (OR = 53.48, 95%CI 37.28 to 69.68, P = 0.0002), the intra-operative blood loss significantly lower (OR = - 266.86, 95%CI - 454.82 to - 78.90, P = 0.005) as were the post-operative complications (OR = 0.40, 95%CI 0.23 to 0.70, P = 0.007) associated to laparoscopy. There was no effect due to laparoscopy on pelvic (OR = 0.62, 95%CI - 1.47 to 2.71, P = 0.560) and para aortic (OR = 1.49, 95%CI - 2.49 to 5.60, P = 0.477) lymph nodal yield, and intra-operative complications (OR = 1.60, 95%CI 0.49 to 5.22, P = 0.390).

In the other meta-analysis by H Zhang et al (44) eight Randomised trials were included, with 3599 patients in total. No significant difference was observed between laparoscopy and laparotomy in overall (odds ratio [OR], 0.96; 95% confidence interval [CI], 0.50–1.82; $P = 0.892$), disease-free (OR, 0.96; 95% CI, 0.50–1.82; $P = 0.892$), or cancer-related (OR, 0.90; 95% CI, 0.27–3.08; $P = 0.871$) survival. More intra-operative complications (OR, 1.33; 95% CI, 1.03–1.73; $P = 0.030$), fewer post-operative complications (OR, 0.59; 95% CI, 0.46–0.75; $P < 0.001$), longer operative time (standardized mean difference [SMD], 0.80; 95% CI, 0.46–1.15; $P < 0.001$), lower blood loss (SMD, –2.29; 95% CI, –3.67 to − 0.91; $P = 0.001$), and shorter hospital stay (SMD, –2.60; 95% CI, –3.47 to − 1.72; $P < 0.001$) were associated with laparoscopy. There was

no significant difference between the groups in pelvic (SMD, 0.22; 95% CI, –0.03 to 0.48; $P = 0.086$) or para aortic (SMD, 0.54; 95% CI, –0.04 to 1.11; $P = 0.067$) lymph node yield.

The conclusion from these studies and meta-analyses is that laparoscopic approach should be considered as safe and effective a procedure as the open surgical approach for patients with early stage endometrial cancer. In spite of longer operative times, the advantages of laparoscopy over traditional laparotomy are seen in reduced intra-operative blood loss and postoperative complications. Similar to the surgical management of colorectal cancers where laparoscopic surgery has been proved to have many short term advantages with equivalent long term oncologic outcomes it will emerge to be a likely alternative to laparotomy for early endometrial cancer.

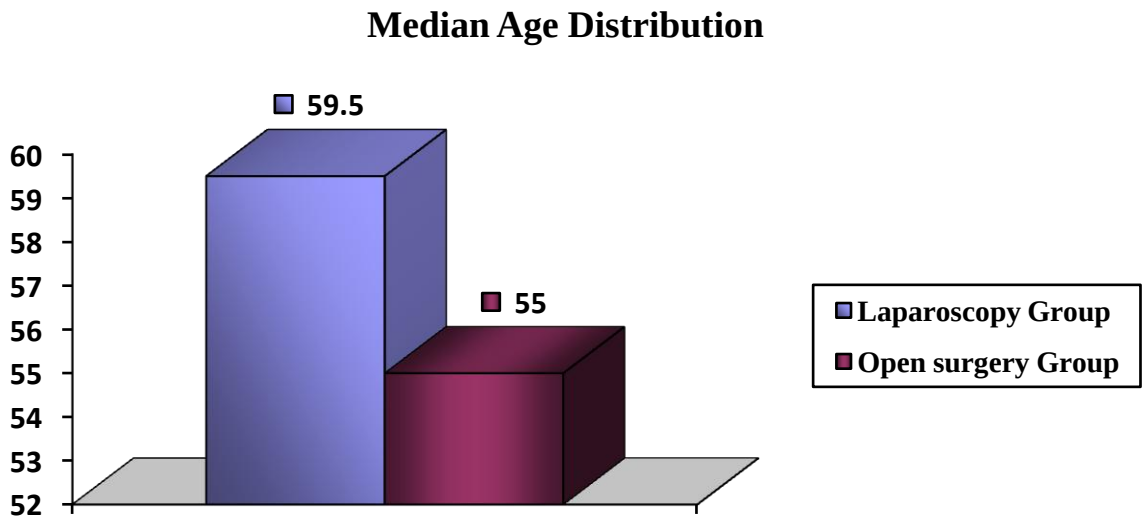
RESULTS

Patient Characteristics

Age Distribution

The median overall age of the patients in our study was 55 years with the laparoscopy group having a median age of 59.5 years and the open group having the median age as 55 years. There was no significant difference in the two groups by independent Samples T-test. (p=0.35)

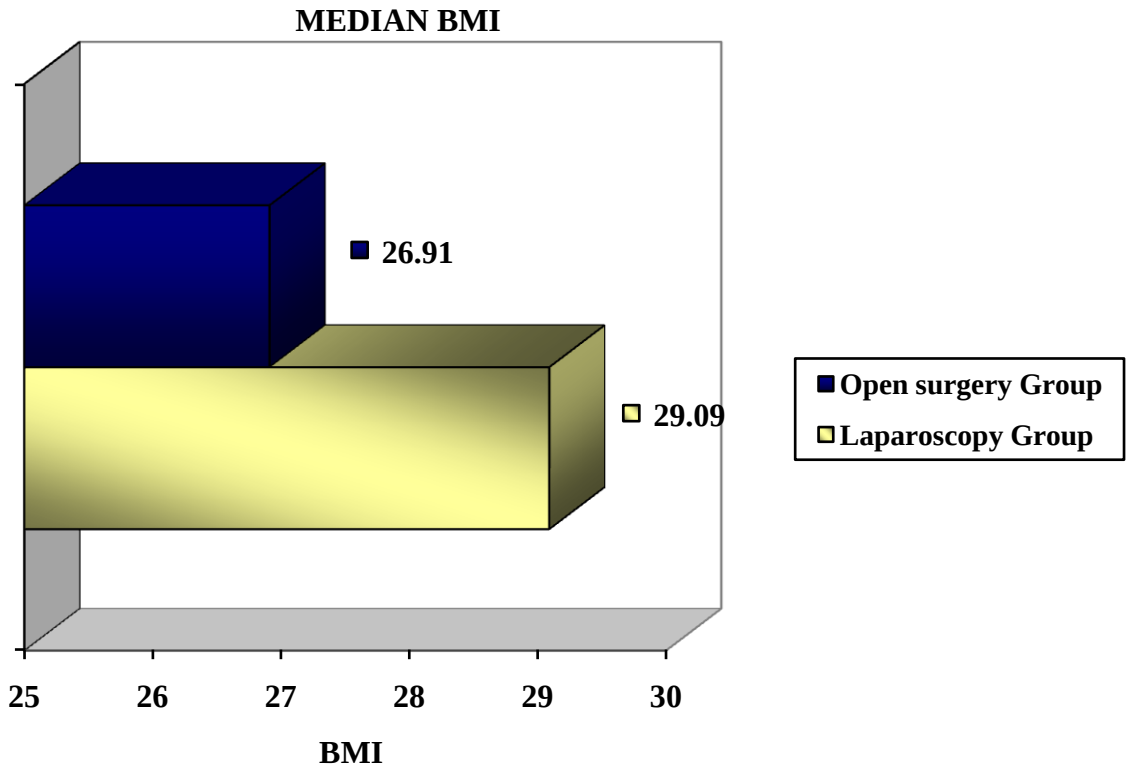
Median Age	Years
Laparoscopy Group	59.5
Open surgery Group	55



Body Mass Index (BMI)

The overall median BMI was 27.82 while in the laparoscopy group it was 29.09 and the open surgical staging group it was 26.91. There was no significant difference in the two groups by independent Samples T-test. (p=0.07)

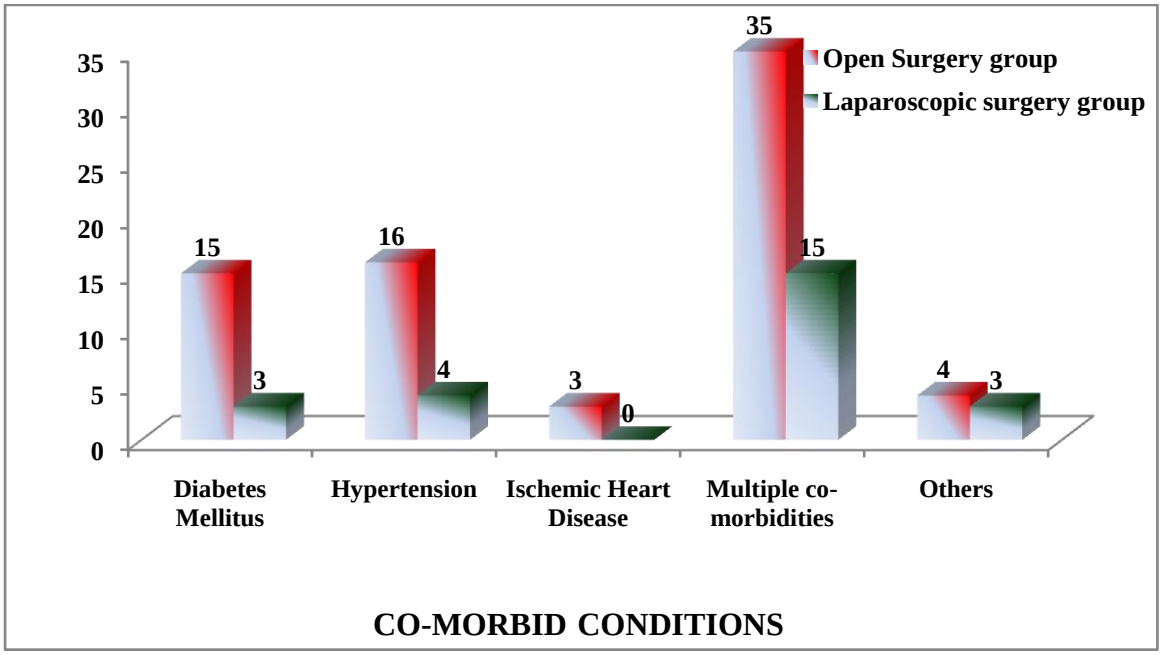
Group	Median BMI
Laparoscopy Group	29.09
Open surgery Group	26.91



Co-Morbid conditions

There was no significant difference in the occurrence of co-morbid illnesses in the two groups (p=0.39)

Co-morbid condition	Open Surgery group	Laparoscopic surgery group
Diabetes Mellitus	15	3
Hypertension	16	4
Ischemic Heart Disease	3	0
Multiple co-morbidities	35	15
Others	4	3

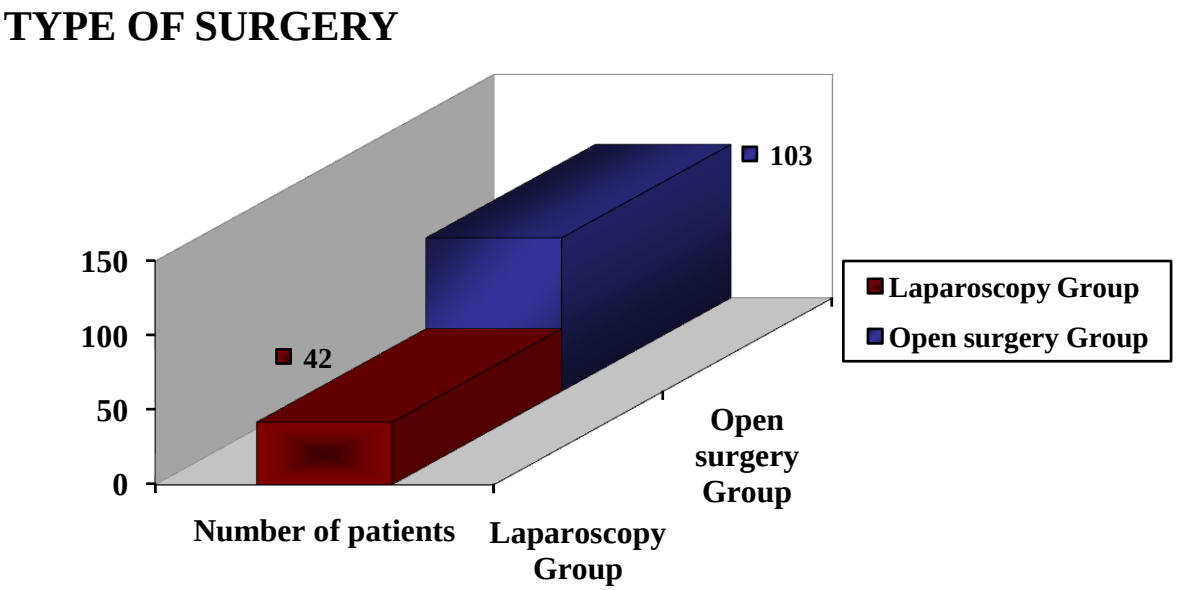


Surgical parameters

Type of surgery

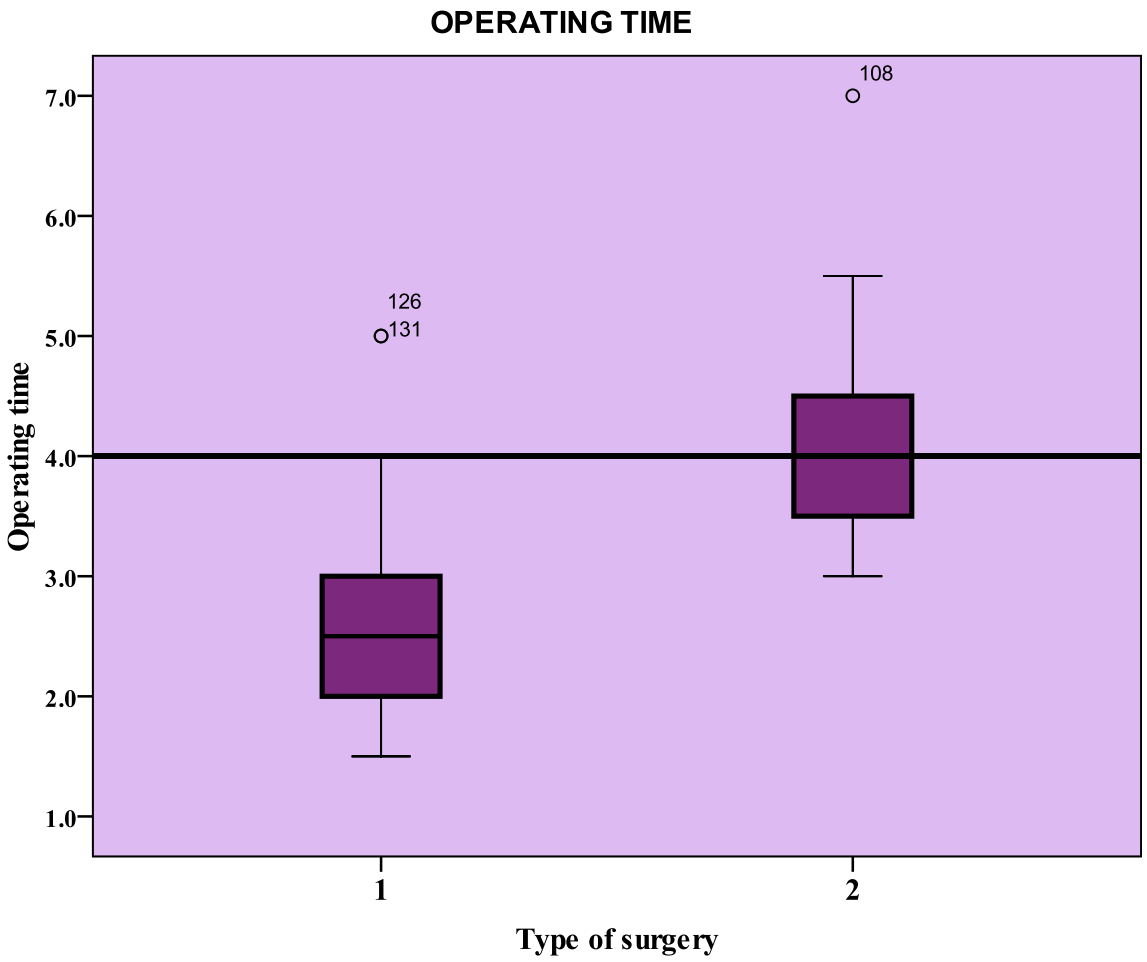
Of the 145 patients operated during the time period from 2006 to 2010, 103 patients underwent open surgical staging while 42 patients were staged laparoscopically.

Group	Number of patients
Laparoscopy Group	42
Open surgery Group	103



Operating time

The median operating time was significantly different in the two groups- it was 4 hours in the laparoscopic surgery group and 2.5 hours in the open surgery group ($p<0.001$).

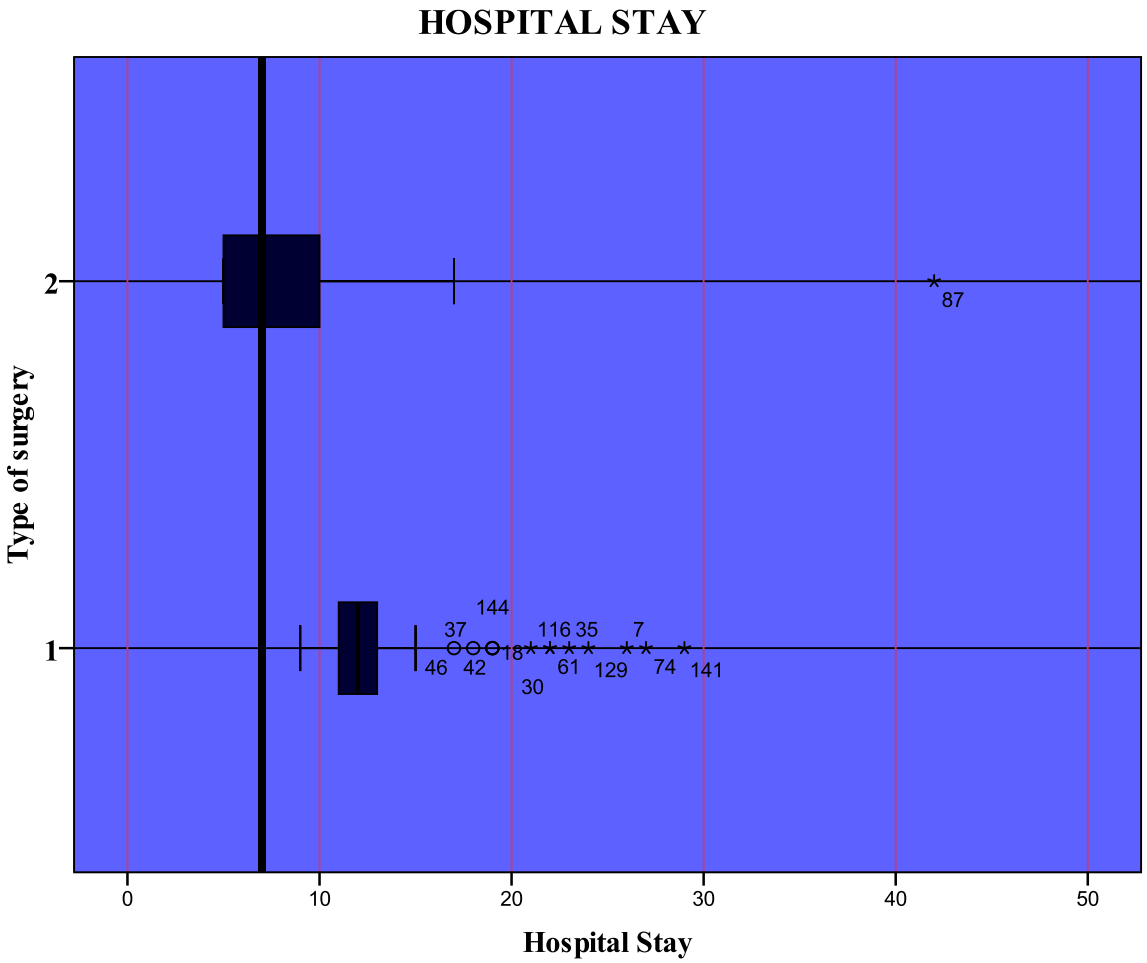


Blood loss

The median blood loss in both the laparoscopic and open surgery patient groups was 300 ml ($p=0.577$)

Hospital Stay

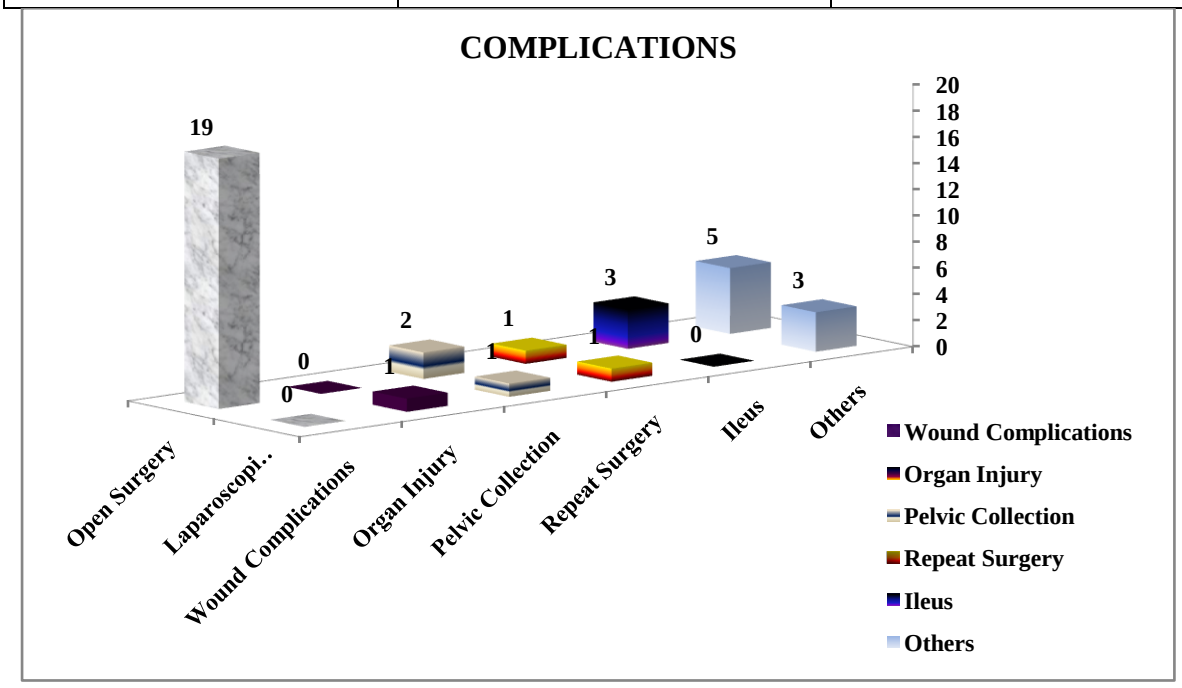
The median duration of hospital stay was 7 days (range 5-42 days) in the laparoscopic surgery group while it was 12 days(range 9-29 days) in the open staging group and it was found to be statistically significant (p<0.001)



COMPLICATIONS

There were 35 complications overall, with 30 occurring in the open surgery group and 5 in the laparoscopic surgery group.

Complication	Open Surgery	Laparoscopic surgery
Wound complications	19	0
Organ Injury	0	1(ureteric injury)
Pelvic collection	2	1
Repeat Surgery	1 (Wound dehiscence repair)	1(ureteric reimplantation)
Ileus	3	0
Others	5	3



There was significant difference (p=0.028) in the incidence of complications between the two groups of patients. The most common complication in the open surgery group was wound infection and re-suturing (19 patients). Pelvic collection occurred in two patients in the open surgery group and in one patient in the laparoscopic staging group. All of these were managed conservatively.

There was one ureteric injury necessitating a ureteric re-implantation in the laparoscopy group. Interestingly all the complications in the laparoscopy group occurred in the first ten patients after which there were no complications. There were two conversions in the laparoscopy group both in view of intra operative bleed. Other complications included urinary tract infection (5 patients), post operative cardiac ischemia (1 patient), atrial flutter (1 patient) and respiratory infection (1 patient). Post operative paralytic ileus delaying oral feeds occurred in three patients who underwent open surgical staging.

The following factors were considered to be confounding factors that may independently increase the occurrence of complications following surgery.

1. Use of pre operative ICA
2. Presence of co-morbid conditions
3. High BMI
4. Long duration of surgery
5. Increased Blood loss
6. Total number of pelvic nodes removed

Univariate and multivariate analysis did not reveal any significant difference in these factors between the two groups essentially proving that the observed difference in the incidence of complications were due to the type of surgical technique used and not due to any other factor.

On subgroup analysis, among patients who underwent open surgical staging, number of pelvic nodes removed was found to be a significant factor in relation to occurrence of complications ($p=0.015$) and in those with laparoscopic staging use of pre-operative ICA was found to be significant ($p=0.035$) on univariate analysis. It was also found that the hospital stay was prolonged in those patients with complications to a significant degree ($p=0.003$ in open surgical staging and $p<0.001$ in laparoscopic staging)

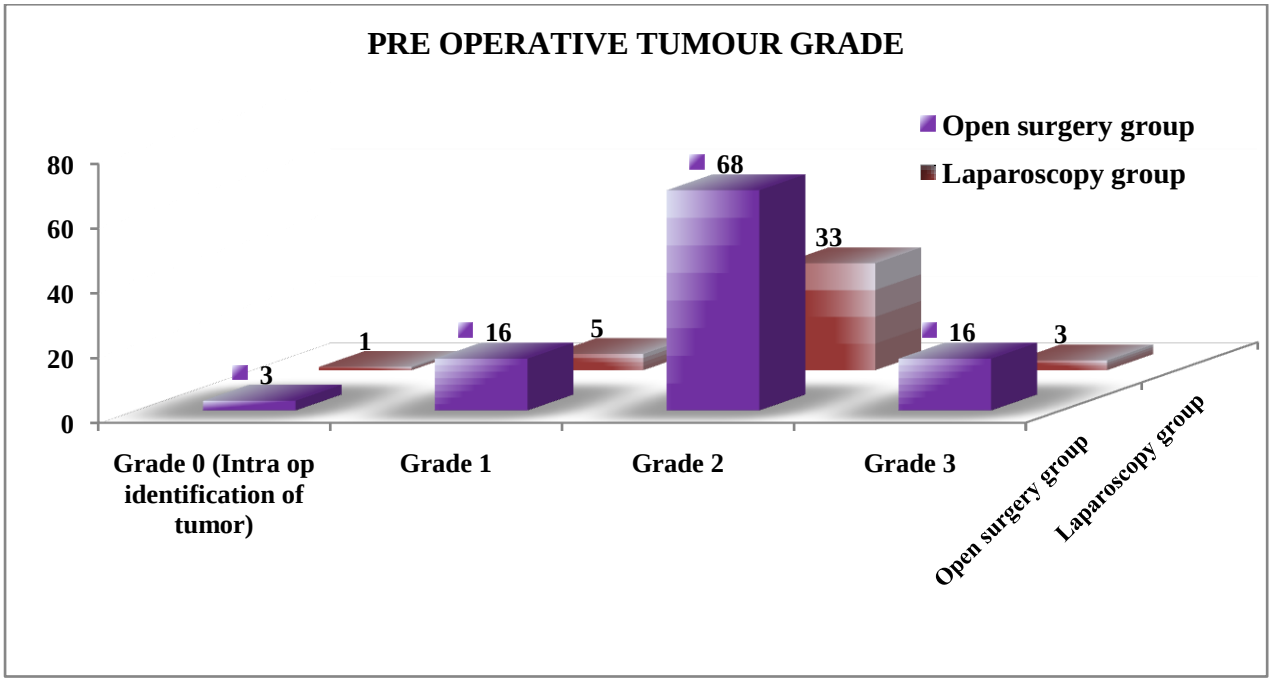
Pathological Parameters

Pre operative Grade

The preoperative grade determined from the biopsy of the lesion showed that grade 2 was the most common grade among both the groups. There was no statistical significant difference in the distribution of grades in the two groups. ($p=0.461$)

In three patients in the open surgical group and one patient in the laparoscopic group, the tumour was identified intra-operatively after a frozen section study of the tumour from the hysterectomy specimen subsequent to which the rest of the staging was completed in the same sitting.

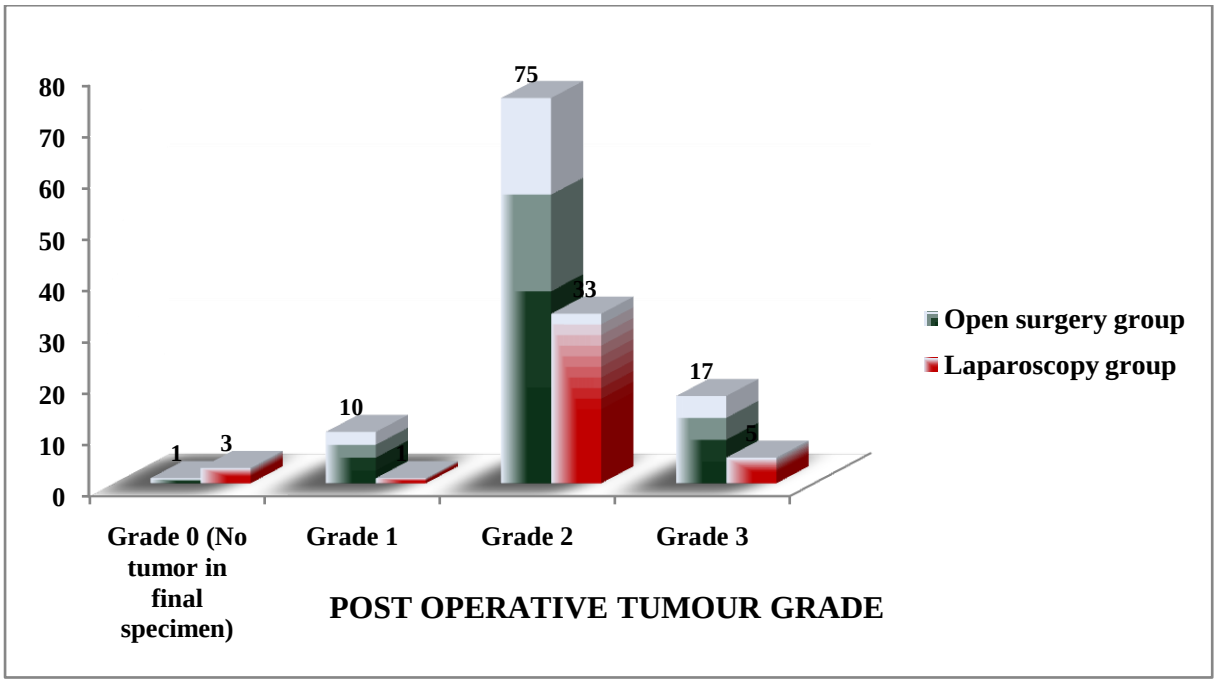
Pre Operative Grade	Open surgery group	Laparoscopy group
Grade 0 (Intra op identification of tumour)	3	1
Grade 1	16	5
Grade 2	68	33
Grade 3	16	3



Post operative grade

There was a change in the post operative grade compared to the pre operative grade in 39 patients. In 15 patients it was downgraded of which 4 patients did not have any tumour in the final resected specimen. For 24 patients there was an escalation of the tumour to a higher grade in the postoperative histopathology highlighting the discordance between pre operative and final grade of the tumour.

Post Operative Grade	Open surgery group	Laparoscopy group
Grade 0 (Intra op identification of tumour)	1	3
Grade 1	10	1
Grade 2	75	33
Grade 3	17	5



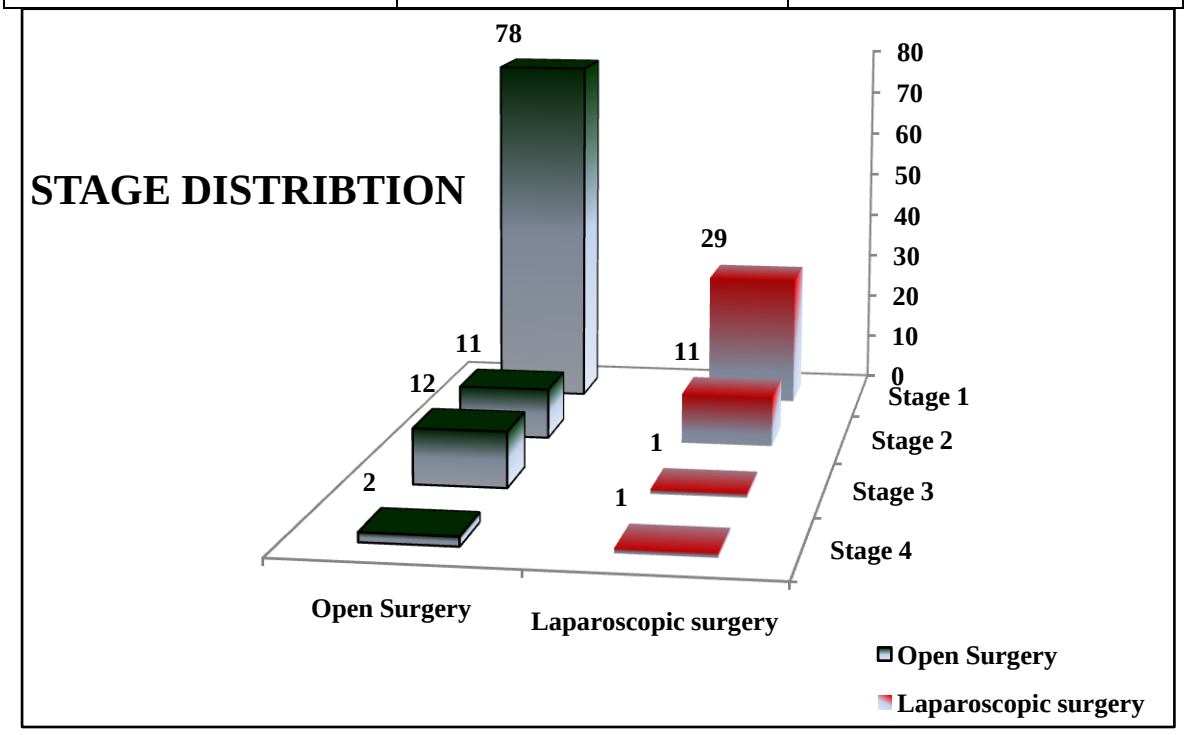
Specimen and tumour size

There was no significant difference in the median size of the uterus specimen (9 cm in the open group vs. 8.5 cm in the laparoscopy group) (p=0.075) or tumour size (Median size 3.5 cm in both groups) (p=0.091) ascertaining that the presence of a bulky uterus is not a deterrent to the performance of laparoscopic staging.

Stage Distribution

Most patients in both groups had Stage 1 endometrial cancer constituting 76% and 69% of the open and laparoscopic groups respectively.

Stage	Open Surgery	Laparoscopic staging
1	78 (76%)	29(69%)
2	11(10.5%)	11(26%)
3	12(11.5%)	1(2.5%)
4	2(2%)	1(2.5%)

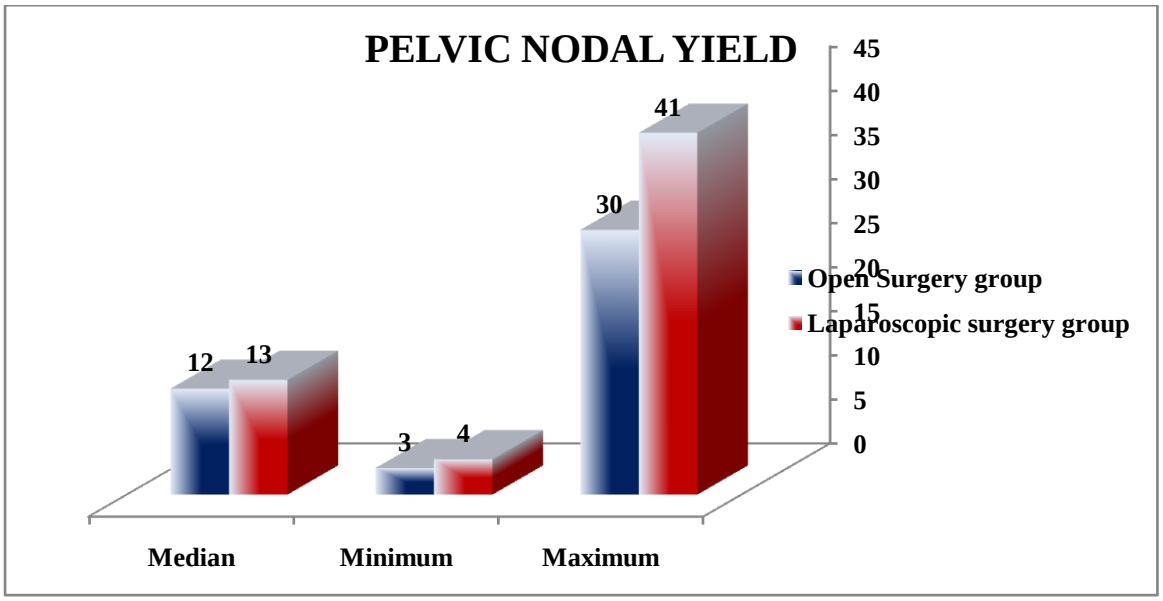


Nodal yield

The median number of pelvic nodes removed in the entire study group was 13 nodes. The median number of pelvic nodes removed in the open surgery group was 12

nodes (range 3 to 30 nodes) and the figure for the laparoscopic surgery group was 13 nodes (range 4 to 41 nodes) (p=0.488 by Independent samples t- test). In the laparoscopic staging group the median number of pelvic nodes removed improved from 10 in the initial 21 cases to 16 in the next 21 cases reflecting the increasing nodal yield with crossing of the learning curve.

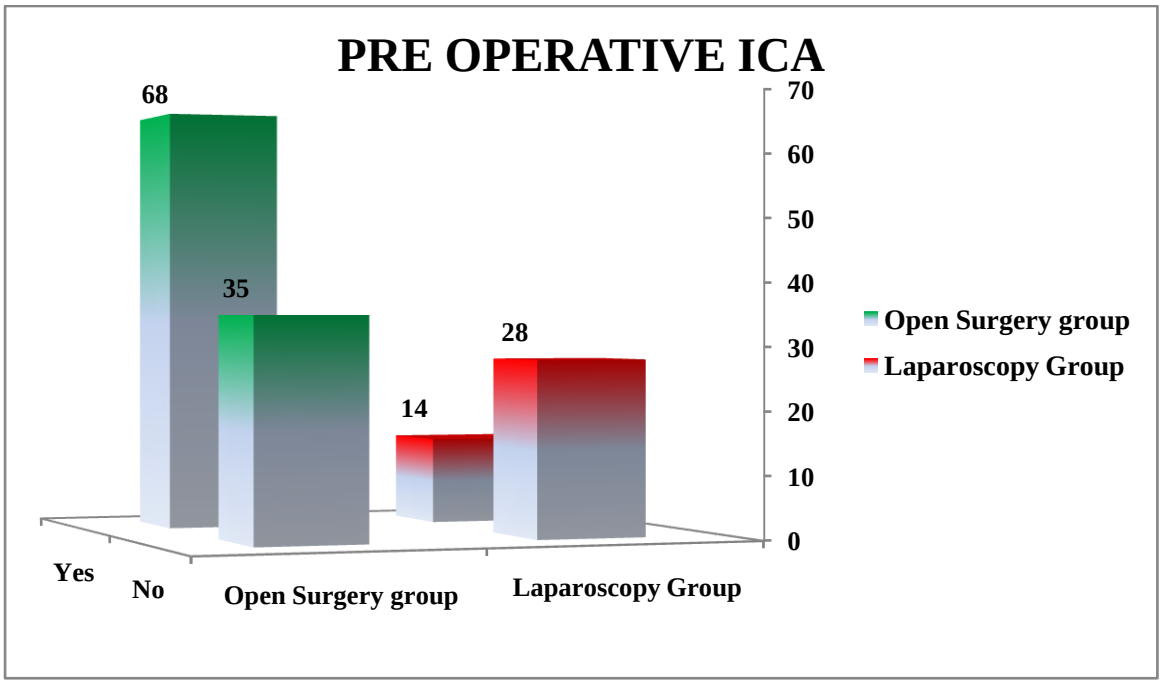
	Open Surgery group	**Laparoscopic surgery group**
Median	12	13
Minimum	3	4
Maximum	30	41



Treatment Parameters

Pre operative Radiation

Patients with high grade histology were treated with one or two sittings of HDR brachytherapy by Intra Cavitary application (ICA). Sixty eight patients in the open surgery group and fourteen patients in the laparoscopic staging group received pre operative ICA.

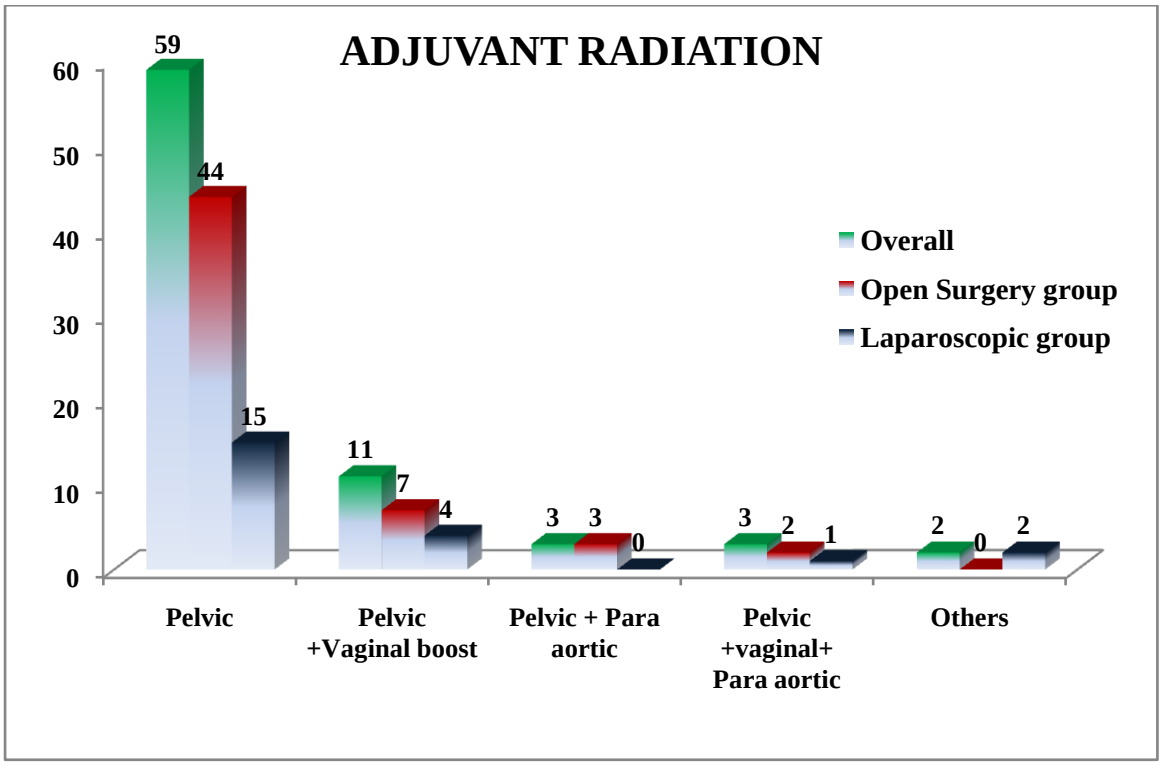


Adjuvant Radiation

Patients with high risk features like deep myometrial invasion, pelvic nodal involvement, cervical involvement or non endometroid histology received adjuvant radiation.

59 patients received external beam pelvic radiation alone while 11 received additional vaginal boost. 3 patients had pelvic and para aortic nodal radiation while a similar number had radiation to all three regions. One patient received vaginal brachytherapy only while one patient was detected to have metastases in the pubic ramus and treated by external beam radiation.

Type of Adjuvant RT	**Overall**	**Open Surgery group**	**Laparoscopic group**
Pelvic	59	44	15
Pelvic +Vaginal boost	11	7	4
Pelvic + Para aortic	3	3	0
Pelvic +vaginal+ Para aortic	3	2	1
Others	2	0	2



Adjuvant Chemotherapy

Doublet chemotherapy with Taxol and carboplatin was used in six patients with gross pelvic nodal positive disease, para aortic nodal disease and omental disease and one patient with a synchronous ovarian malignancy while carboplatin alone was used in one patient with gross pelvic nodal disease.

Tamoxifen induced endometrial cancer

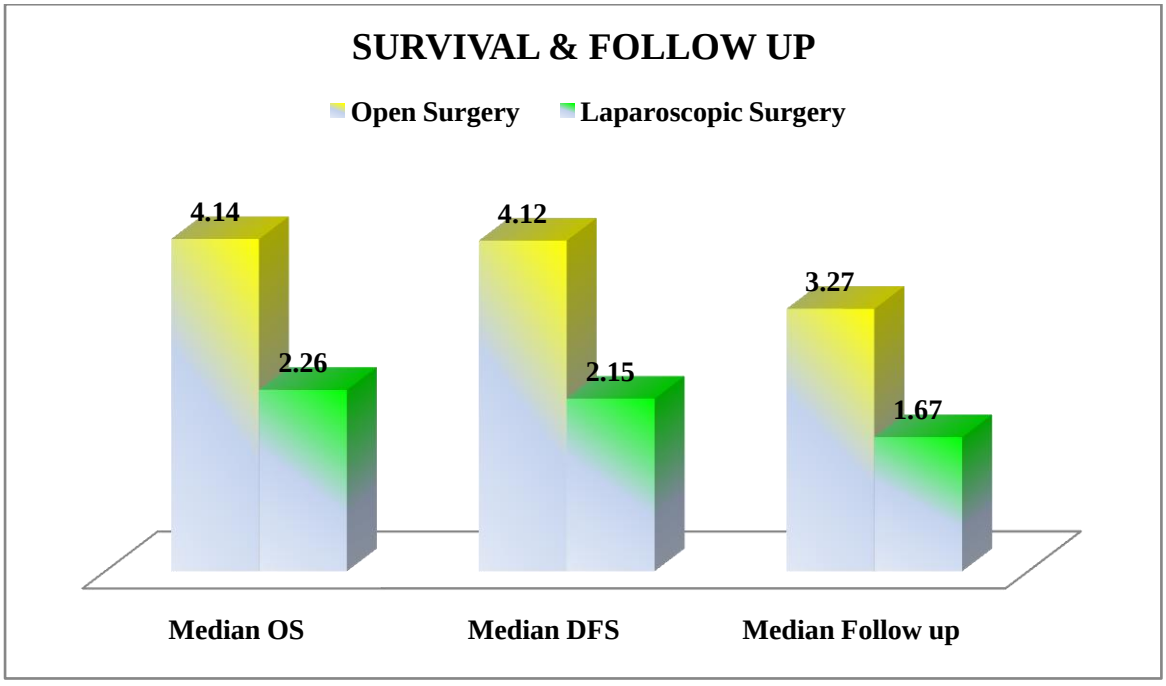
Tamoxifen induced endometrial cancer constituted 8.3% of the entire study population. There were twelve patients who had previously been treated for carcinoma breast and presented with tamoxifen induced endometrial carcinoma. The median duration of tamoxifen use was 5 years. (Range 2 to 10 years). The median time to

develop to uterine malignancy after treatment of carcinoma of the breast was 5 years (range 2 to 14 years).

SURVIVAL ANALYSIS

Overall Survival (OS)

The overall survival was calculated from the date of completion of treatment to the date of last follow up in all patients who are still alive or are lost to follow up and from the date of completion of treatment to the date of death in all patients in the study whom death occurred due to any cause.



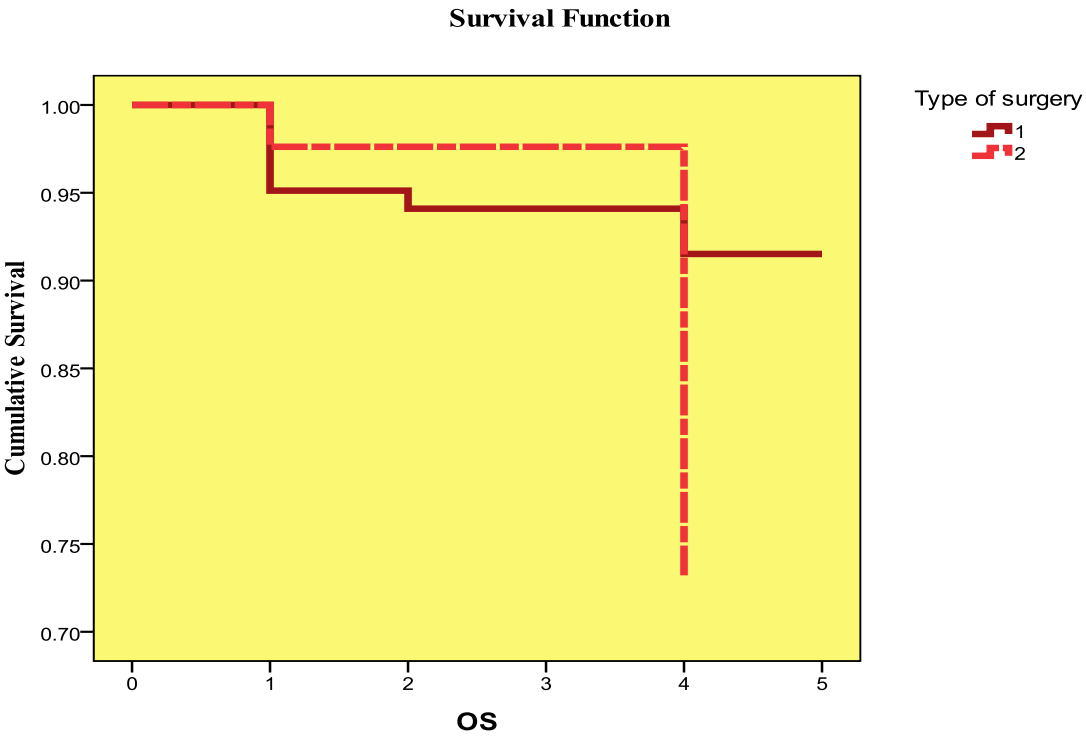
The median Overall Survival (OS) in the laparoscopy group was 2.26 years and 4.14 years in the open surgical group. This was not statistically significant when the

analysis was done by life table method. (p=0.735). The shorter overall survival in the laparoscopy surgery is due to the fact that laparoscopic surgery was done only from 2008 and the median follow up was only 1.67 years whereas it was 3.27 years for the open surgery group

Type 1 = Open Surgery Type 2 = Laparoscopic Surgery

Life Table for Overall Survival – P=.735

First-order Controls	Interval Start Time		Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval
Type of surgery	1	0	103	1	102.500	5	.05	.95	.95
		1	97	9	92.500	1	.01	.99	.94
		2	87	6	84.000	0	.00	1.00	.94
		3	81	16	73.000	2	.03	.97	.92
		4	63	37	44.500	0	.00	1.00	.92
		5	26	26	13.000	0	.00	1.00	.92
	2	0	42	0	42.000	1	.02	.98	.98
		1	41	16	33.000	0	.00	1.00	.98
		2	25	18	16.000	0	.00	1.00	.98
		3	7	6	4.000	1	.25	.75	.73



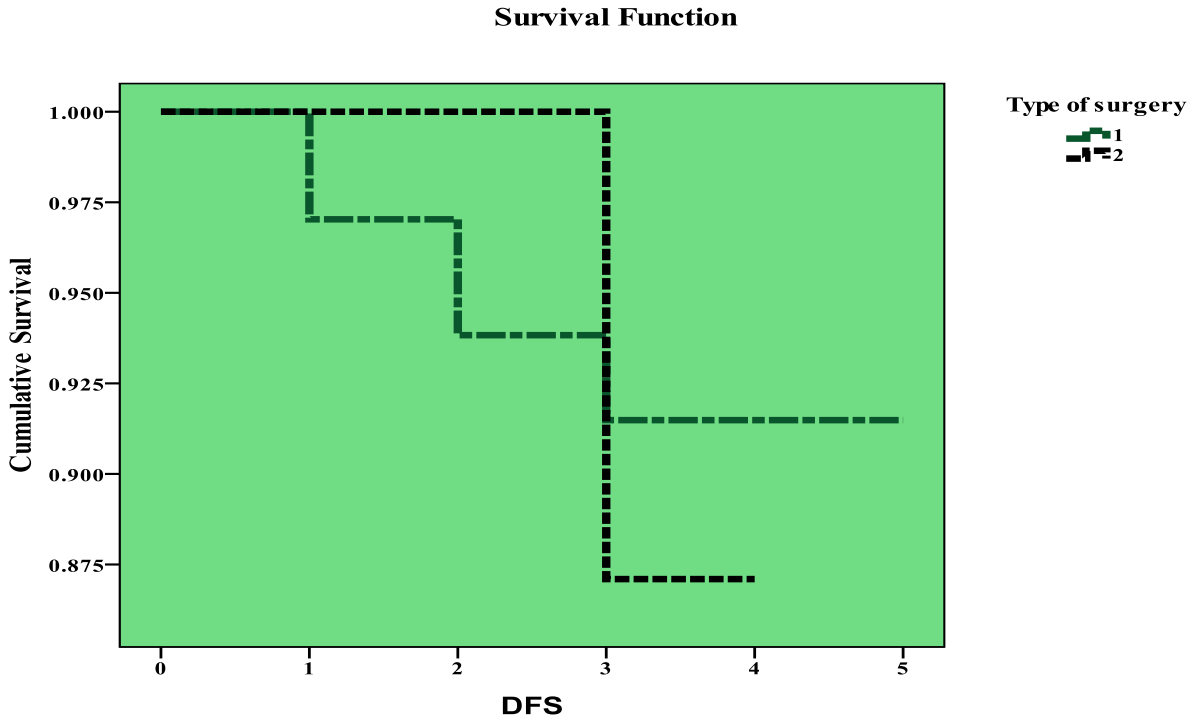
Disease Free Survival

The DFS was calculated from the date of completion of treatment to the date of recurrence in patients with recurrences and from date of completion of treatment till the date of last follow up in all other patients. The median DFS for the laparoscopic surgery group and the open surgery group were 2.15 and 4.12 years respectively. Life table method did not show any statistical significance. (p=0.589)

Type 1 = Open Surgery Type 2 = Laparoscopic Surgery

Life Table for Disease Free Survival – P=0.589

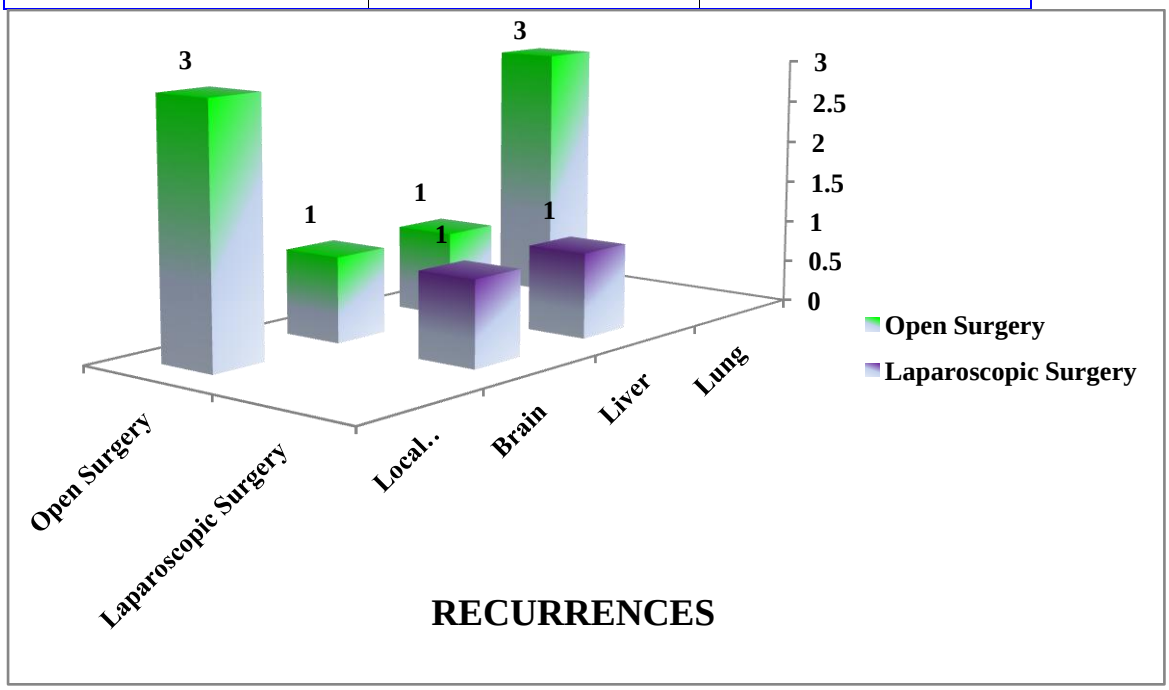
First-order Controls	Interval Start Time		Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval
Type of surgery	1	0	34	1	33.500	1	.03	.97	.97
		1	32	9	27.500	1	.04	.96	.93
		2	22	6	19.000	1	.05	.95	.89
		3	15	15	7.500	0	.00	1.00	.89
	2	0	42	1	41.500	1	.02	.98	.98
		1	40	16	32.000	0	.00	1.00	.98
		2	24	17	15.500	2	.13	.87	.85
		3	5	5	2.500	0	.00	1.00	.85



Recurrences

Other than the three patients who died of advanced disease there were seven recurrences – a total of eight in the open surgery group and two in the laparoscopy group. There were three regional recurrences that occurred in the pelvic nodes which were salvaged by radiation in the laparotomy group. There was no significant difference in the recurrence rate (p=0.517) in the two groups.

Site	Open Surgery	Laparoscopic Surgery
Lung	3	
Liver	1	1
Brain	1	1
Regional recurrence	3	

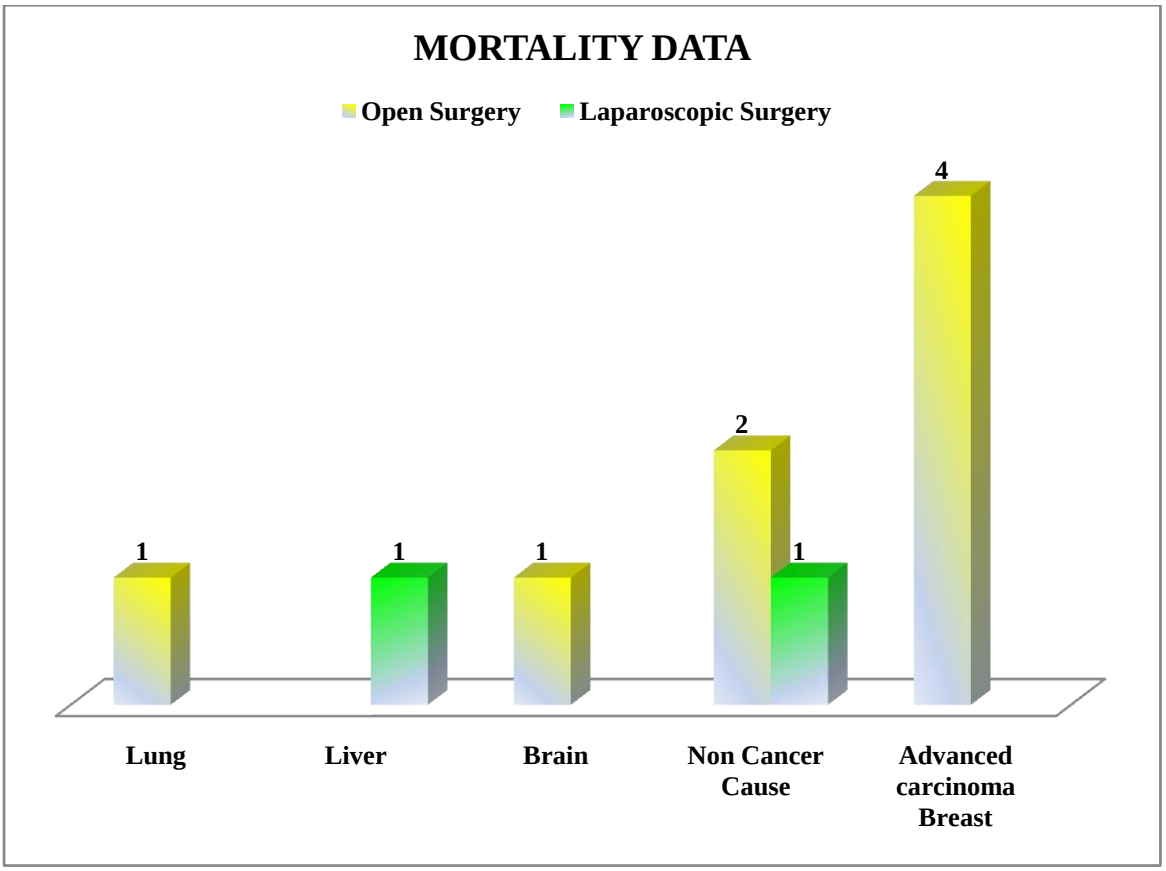


MORTALITY

There were ten deaths in the study population eight in the open surgery group and two in the laparoscopic surgery group. Of the ten deaths, two were not related to malignancy and four were due to metastatic carcinoma breast in patients who developed carcinoma endometrium after previous treatment for carcinoma breast.

In one patient the cause of death was not known. In the three attributable to advanced carcinoma endometrium, death was as a result of lung, brain and liver metastases respectively.

	Open Surgery	Laparoscopic Surgery
Lung	1	
Liver		1
Brain	1	
Non Cancer Cause	2	1
Advanced carcinoma Breast	4	


MORTALITY DATA
Open Surgery
Laparoscopic Surgery
1
1
1
2
1
4
Lung
Liver
Brain
Non Cancer Cause
Advanced carcinoma Breast

DISCUSSION

The median age of our study population was 55 years (Range 30-79 years) and not statistically different between the laparoscopy (median 59.9 years, range 32-79years) and open surgery (median 55 years, range 30-77 years) groups. In the studies in Western population by Eltabbakh et al (35), Ghezzi et al. (45) Volpi et al (46) the median age was about 63 years whereas in the studies on Asian population like Lee et al (47) and Tay (48) the median age was similar to our study being about 51 years.

In the Western studies mentioned above, the study population tended to have higher BMI of more than 30 while in our study it was 28 which was closer to the value of around 26 in the data on Asian patients by Lee et al (47) and Tay (48). This probably reflects the geographic difference in the study population. In contrast to most of the above mentioned studies where the median BMI tended to be lower in the laparoscopy group, in our study the median BMI was higher in the laparoscopy group (median 29, range 19-39) than in the open surgery group (median 27, range 16-53) though it did not reach statistical significance ($p = 0.07$)

Our median operating time for laparoscopic staging was 4 hours (range 3-7 hours) and 2.5 hours for the open surgery group (range 2-5 hours). In comparison to the studies by Lee et al (47) and Eltabbakh et al (35) it was longer by about 60 minutes probably

reflecting our learning curve as laparoscopic surgical staging was started in our institute only in 2008.

The estimated median blood loss in our study was 300 ml in both the groups (range 100 to 1200ml for open surgery group and 50-800 ml for the laparoscopy group). Post operative blood transfusion was required in 2 patients in the laparoscopy group (4.7%). This was more than the blood loss of 150 ml mentioned by Eisenhauer et al (49) but comparable to the blood loss of about 280-300ml mentioned by Lee et al (50), Eltabbakh et al (35). Our blood loss has been comparatively higher in the laparoscopy group again reflecting our learning curve for the procedure.

The median hospital stay was significantly less in the laparoscopic staging group at 7 days (range 5-42 days) compared to the open surgical group at 12 days (range 9-29 days). These results were consistent with the various studies quoted above showing a shorter post operative stay for laparoscopic staging thus demonstrating that laparoscopic technique is associated with earlier discharge from the hospital. Studies also showed that laparoscopy is associated with earlier return to normal activity compared to laparotomy as well as reduced total overall costs. (Spirtos et al. 51) (Gemignani et al. 52)

In the LACE study, (53) in the early recovery phase (upto four weeks post surgery), patients with laparoscopic hysterectomy experienced a clinically and statistically significantly greater improvement in most Quality of life measurements, compared to patients receiving open surgery. During the late post-operative recovery

phase (3 to 6 months post surgery), patients with laparoscopic surgery compared to patients with open surgery recovered significantly more in their physical (p=0.008), functional (p=0.009), endometrial cancer-specific (p=0.003), and overall well-being (FACT-G) (p = 0.03), and also experienced superior Quality of life recovery with regards to body image (p=0.001).

There was significant difference (p=0.028) in the incidence of complications between the two groups of patients in our study with 30 complications (29.1%) in the laparotomy group and 5 in the laparoscopy group (11.9%). There was no wound related morbidity in the laparoscopy group.

The complications in the laparoscopy included two cardiac related events, one pelvic collection, one ureteric injury and re-implantation and one urinary infection, thus leading to only two surgery-related complications. This was similar to the reported complication rates for laparoscopic surgery by Eltabbakh et al (35) - 10.5%, more than the reports by Gemignani et al. (52) – 5.8%, Childers et al. – 5.1% (26), but less than that reported by Boike et al - 25% (54) and Magrina et al. (55)

In the laparotomy group, there were 19 surgical site wound problems some of them needing secondary suturing and thus prolonging hospital stay. There was one patient with burst abdomen needing tension repair. One late post- operative complication

occurred in the form of obstructed incisional hernia needing emergency re-exploration and repair. Post operative ileus occurred in 3 patients causing a stoppage of and re-initiation of oral feeds.

Two patients developed pelvic collections which were managed conservatively. The other complications in this group were related to urinary or respiratory infection and cardiac related events.

It was also found that in both groups the hospital stay was significantly prolonged in both the groups in those patients in whom complications occurred. ($p=0.003$ in open surgical staging and $p<0.001$ in laparoscopic staging) As a direct consequence of this, the potential for prolonged hospital stay as a result of complications is also reduced. Also laparoscopic surgical staging significantly reduced complications especially surgical site infection.

The conversion rate to laparotomy in our study was 4.76% i.e. in two patients, both due to intra-operative bleed. The rates quoted were Gemignani et al. (52) - 4.3%, Eltabbakh et al (35) – 5.8%, Childers et al. – 13.6% (26), Boikee et al – 13% (54), and Spirtos et al.-0% (51). The conversion rate is comparable to that mentioned in the above studies and is bound to come down with the experience of the surgeon though excessive adhesions, bleed obscuring vision or cardiopulmonary problems intra-operatively due to

increased positive pressure induced by insufflation still occasionally necessitate conversion.

Among the pathological parameters analysed, the median size of the uterus specimen was 9 cm (range 5-16 cm) in the open surgery group and 8.5 cm (range 7-13 cm) in the laparoscopy group (p=0.075). In all patients the specimen was delivered per vaginum and there was no patient who required a mini laparotomy to deliver the specimen. There was no evidence of vagina or parametrial margin positivity on pathological examination.

The median pelvic nodal yield in our study was 13 in the laparoscopic surgery group (range 4-41) and 12 in the open surgery group (range 3-30) and the difference was not statistically significant (p=0.488). Subgroup analysis revealed that the pelvic nodal yield in the laparoscopic surgery group improved from a median of 10 nodes in the initial 21 surgeries to 16 in the next 21 patients.

The pelvic nodal yield mentioned in various studies is comparable viz. Eltabbakh et al – 10.8 (39), Ghezzi et al. - 18 (45), Volpi et al – 15.9 (46), Eisenhauer et al – 15 (49) and Malur et al. – 16.1 (36). The other studies also mention the improvement in the nodal yield with surgeon experience.

The most common pathological stage was Stage I in both open and laparoscopic surgery group 76% in open staging and 69% in the laparoscopy group. This is in concordance with the natural history of the disease and the percentages mentioned in various studies where Stage I tumours were the commonest stage at presentation (Tay et al. - 92% (48), Eltabbakh et al – 80.2% (35), Ghezzi et al. - 83.8% (45), Volpi et al – 82.9% (46) and Eisenhauer et al – 92% (49). Many of the Western studies had a higher representation of stage I disease probably because of earlier identification of the malignancy compared to our study population because of greater awareness and the early reporting to health care providers in the Western setup.

The analysis of disease free and overall survival in our study was the secondary objective. The median follow-up for the laparoscopy group was 1.67 years (range 0.1 to 3.26) and 3.27 years for the laparotomy group (range 0.1 to 5.78). The difference is also seen in many of the retrospective studies - Eltabbakh et al – 24 and 48 months (35), and Ghezzi et al. - 52 and 80 months (45).

Previous studies have shown that 76% of the recurrences occur within the first three years. The median time to recurrence was 14 months for patients with local recurrence and 19 months for those with distant metastases (56). In our study there were 10 recurrences, eight in the open surgery group (7.7%) and two (4.76%) in the laparoscopic staging group. There were no local recurrences in the laparoscopy group – one patient had lung metastases and the other had brain metastases. Among the patients in open surgery group, there were three regional recurrences that were salvaged by

radiation. The difference in the site and incidence of recurrences was not statistically significant.

The recurrence rates reported by other authors with similar studies were 7% and 10.5% for by Eltabbakh et al (35), 11.1% and 15.6% by Ghezzi et al. (45), and 9% and 11% by Magrina et al. (55).

The two year DFS for the open and laparoscopic surgery groups was 98% and 96% respectively while the 2 year OS was 98% and 94% respectively. There were ten deaths in our study population – eight in the open surgery group and two in the laparoscopic surgery group. The cause specific mortality was 2.75%. Only four deaths were attributable to advanced carcinoma endometrium. Four deaths were due to progression of carcinoma breast in patients who developed tamoxifen induced endometrial cancers and two deaths were not related to cancer.

CONCLUSION

Carcinoma endometrium is showing a rising incidence in our country. The essential management of this malignancy is surgical with extended staging being the recommendation for all patients. The surgical staging is traditionally accomplished by laparotomy but the advent of laparoscopy has made possible this minimally invasive option to be used for achieving the same ends.

The median age of our study population is about 8 years lower than that of the Western world. Also our patients tend to have a lower BMI and there is no impact of BMI on the ability to perform a safe laparoscopic staging. There is no statistically significant difference in the use of laparoscopy in patients with co-morbid conditions.

Laparoscopic surgery results in significant reduction in hospital stay and incidence of complications especially surgical site infections and paralytic ileus. While it is associated with a significantly prolonged operating time, there is no difference in the median blood loss compared to open surgery.

The grade and stage distribution are comparable in the laparotomy and laparoscopy groups and the pelvic nodal yield is equal if not better in the latter group. There is also a trend towards improving nodal yield with the increasing surgical experience of the operating surgeon.

Though long term data are not available, short term results show that there is no significant difference in the 2-year overall survival and disease free survival between the two groups nor do they show any statistically significant difference in the recurrence rate or disease specific mortality.

Similar to colorectal cancers where laparoscopic surgery has been proved to have short term advantages with equivalent long term oncologic outcomes, the laparoscopic surgical staging in carcinoma endometrium can be performed as safely as the conventional open approach without compromising on the operative, pathological and oncologic outcomes and has the added advantage of fewer complications and decreased hospital stay.

BIBLIOGRAPHY

1. Swaminathan R, Shantha V, Balasubramanian S, Sampath P. Cancer Incidence and mortality in Chennai , India 2006-2008. National Cancer Registry Program, Cancer Institute (WIA), Chennai, 2010
2. Parazzini F, LaVecchia C, Bocciolone L, Franceschi S. The epidemiology of endometrial cancer. Gynecol Oncol 1991;41:1-16.
3. Prat J, Gallardo A, Cuatrecasas M, Catasus L. Endometrial carcinoma: pathology and genetics. Pathology 2007;39:1-7.
4. Creasman WT, Odicino F, Mausinneuve P, Quinn MA, Beller U, Benedet JL et al. Carcinoma of the corpus uteri. FIGO Annual Report, Vol 26. Int J Gynaecol Obstet 2006;95(suppl 1):S105-S143.
5. Hacker NF, Moore JG, Gambone JC eds. Essentials of obstetrics and gynecology, 4th ed. Philadelphia: Elsevier, 2004:479
6. FIGO Committee on Gynecologic Oncology. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynecol Obst 2009;105:103-104.
7. DeVita, Vincent T.; Lawrence, Theodore S.; Rosenberg, Steven A. Devita, Hellman & Rosenberg's Cancer: Principles & Practice of Oncology, 8th Edition. . ©Lippincott Williams & Wilkins. 2008: 1545-48
8. Heyman J, Reuterwall O, Benner S: The Radiumhemmet experience with radiotherapy in cancer of the corpus of the uterus: Classification, method of treatment , and results . Acta Radiol 22:11-98, 1941.

9. Sause WT, Fuller DB, Smith W, et al: Analysis of preoperative intracavitary cesium application vs postoperative external-beam radiation in stage I endometrial carcinoma. Int J Radiat Oncol Biol Phys 18: 1011-1017, 1990.
10. Weigensberg IJ: Preoperative radiation therapy in stage I endometrial adenocarcinoma. II . Final report of a clinical trial. Cancer 53:242-247, 1984.
11. Lee NK, Cheung MK, Shin JY, Husain A, Teng NN, Berek JS, et al. Prognostic factors for uterine cancer in reproductive-aged women. Obstet Gynecol 2007;109:655-662.
12. Christopherson WM, Alberhasky RG, Connelly PJ. Carcinoma of the endometrium: I. a clinicopathologic study of clear cell carcinoma and secretory carcinoma. Cancer 1982;49:1511-1516.
13. Sherman ME, Bitterman P, Rosenshein NB, Delgado G, Kurman RJ. Uterine serous carcinoma. Am J Surg Pathol 1992;16:600-610.
14. Abeler VM, Vergote IB, Kjorstad KE, Trope CG. Clear cell carcinoma of the endometrium. Cancer 1996;78:1740-1747.
15. Hamilton CA, Cheung MK, Osann K, Chen L, Teng NN, Longacre TA, et al. Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers. Brit J Cancer 2006;94:642-6.
16. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. Cancer 1987;60:2035-2041
17. Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma. Obstet Gynecol 1980;56:419-424.

18. Milosevic MF, Dembo AJ, Thomas GM. The clinical significance of malignant peritoneal cytology in stage I endometrial carcinoma. Int J Gynecol Cancer 1992;2:225-235.
19. Liao BS, Twiggs LB, Leung BS, Yu WCY, Potish RA, Prem KA. Cytoplasmic estrogen and progesterone receptors as prognostic parameters in primary endometrial carcinoma. Obstet Gynecol 1986; 67: 463-467.
20. Christopherson WM, Connelly PJ, Alberhasky RC. Carcinoma of the endometrium: V. an analysis of prognosticators in patients with favorable subtypes and stage I disease. Cancer 1983;51:1705-1710.
21. Susini T, Amunni G, Molino C, Carriero C, Rapi S, Branconi F, et al. Ten-year results of a prospective study on the prognostic role of ploidy in endometrial carcinoma. Cancer 2007;109:882-890.
22. Schink JC, Lurain JR, Wallemark CB, Chmiel JS. Tumour size in endometrial cancer: a prognostic factor for lymph node metastasis. Obstet Gynecol 1987;70:216-219.
23. International Federation of Gynecology and Obstetrics. Annual report on the results of treatment in gynecologic cancer. Int J Gynecol Obstet 1989;28:189-190
24. Dargent D, Salvat J. Envahissenent ganglionnaire pelvien: place de la pelviscopie retroperitoneale. Paris: Medsi, McGraw-Hill, 1989.
25. Childers J, Surwit E. A combined laparoscopic vaginal approach in the management of stage I endometrial cancer. Gynecol Oncol 1991;45:46-51.
26. Childers J, Brzechffa P, Hatch K, Surwit E. Laparoscopically assisted surgical staging (LASS) of endometrial cancer. Gynecol Oncol 1992;51:33-38.

27. Childers J, Hatch K, Tran A-H, Surwit E. Laparoscopic paraaortic lymphadenectomy in gynecologic malignancies. Obstet Gynecol 1993;82:741-747
28. Spirtos NM, Schlaerth JB, Spirtos TW, Schlaerth AC, Indman PD, Kimball RE. Laparoscopic bilateral pelvic and paraaortic lymph node sampling: an evolving technique. Am J Obstet Gynecol 1995;173:105-111.
29. Köhler C, Klemm P, Schau A, Possover M, Krause N, Tozzi R, et al. Introduction of transperitoneal lymphadenectomy in a gynecologic oncology center: analysis of 650 laparoscopic pelvic and/or paraaortic transperitoneal lymphadenectomies. Gynecol Oncol 2004; 95:52-61.
30. Querleu D, Leblanc E, Cartron G, Narducci F, Ferron G, Martel P. Audit of preoperative and early complications of laparoscopic lymph node dissection in 1000 gynecologic cancer patients. Am J Obstet Gynecol 2006;195:1287-1292.
31. Spirtos N, Schlaerth J, Gross GM, Spirtos TW, Schlaerth AC, Ballon SC. Cost and quality of life analyses of surgery for early endometrial cancer: laparotomy versus laparoscopy. Am J Obstet Gynecol 1996;174:1795-1799.
32. Melendez TD, Childers JM, Nour M, Harrigill K, Surwit EA. Laparoscopic staging of endometrial cancer: the learning experience. J Soc Laparoendosc Surg 1997;1:45-49.
33. Holub Z, Bartos P, Jabor A, Eim J, Fischlova D, Kliment L. Laproscopic surgery in obese women with endometrial cancer. J Am Assoc Gynecol Laparosc 2000;7:83-88.
34. Eltabbakh GH, Shamonki MI, Moody JM, Garafano LL. Hysterectomy for obese women with endometrial cancer: laparoscopy or laparotomy? Gynecol Oncol 2000;78:329-335.
35. Eltabbakh GH. Analysis of survival after laparoscopy in women with endometrial carcinoma. Cancer 2002; 95:1894-1901.

36. Malur S, Possover M, Michels W, Schneider A. Laparoscopicassisted vaginal versus abdominal surgery in patients with endometrial cancer—a prospective randomized trial. Gynecol Oncol 2001; 80:239-244.

37. Obermair A, Manolitsas TP, Leung Y, Hammond IG, McCartney AJ. Total laparoscopic hysterectomy for endometrial cancer: patterns of recurrence and survival. Gynecol Oncol 2004; 92:789-793.

38. Zapico A, Fuentes P, Grassa A, Arnanz F, Otazua J, Cortés-Prieto J. Laparoscopic-assisted vaginal hysterectomy versus abdominal hysterectomy in stages I and II endometrial cancer. Operating data, follow up and survival. Gynecol Oncol 2005;98:222-227.

39. Kalogiannidis I, Lambrechts S, Amant F, Neven P, Van Gorp T, Vergote I. Laparoscopy-assisted vaginal hysterectomy compared with abdominal hysterectomy in clinical stage I endometrial cancer: safety, recurrence, and long-term outcome. Am J Obstet Gynecol 2007;196:248.e1-8.

40. Tozzi R, Malur S, Koehler C et al. Laparoscopy versus laparotomy in endometrial cancer: first analysis of survival of a randomized prospective study. J Minim Invasive Gynecol 2005;12:130–136.

41. L. Walker, Marion R. Piedmonte, Nick M. Spirtos, Scott M. Eisenkop, John B. Schlaerth, Robert S. Mannel. Laparoscopy ComparedWith Laparotomy for Comprehensive Surgical Staging of Uterine Cancer: Gynecologic Oncology Group Study LAP2. J Clin Oncol 2009;27:5331-5336.

42. L. Walker, Marion R. Piedmonte, Nick M. Spirtos, Scott M. Eisenkop, John B. Schlaerth, Robert S. Mannel. Recurrence and Survival after Random Assignment to Laparoscopy

Versus Laparotomy for Comprehensive Surgical Staging of Uterine Cancer: Gynecologic Oncology Group LAP2 Study. 10.1200/JCO.2011.38.8645 (Online Publication ahead of print)

43. Palomba, S , Falbo, A , Mocciaro, R , Russo, T , Zullo, F et al. Laparoscopic treatment for endometrial cancer: A meta-analysis of randomized controlled trials (RCTs) Gynecol Oncol 2009; 112: 415-421
44. Hui Zhang, Jing Cui, Lin Jia, Shuhui Hong, Beihua Kong, Dadong Li. Comparison of laparoscopy and laparotomy for endometrial cancer. Int J Gynecol Obstet 2012;116:185-191
45. Laparoscopic Versus Open Surgery for Endometrial Cancer: a Minimum 3-Year Follow-Up Study. Fabio Ghezzi, Antonella Cromi, Stefano Uccella, Gabriele Siesto, Silvia Giudici, Maurizio Serati, Massimo Franchi. Ann Surg Oncol (2010) 17:271–278
46. Laparoscopic treatment of endometrial cancer: feasibility and results. Eugenio Volpi, Annamaria Ferrero , Maria Elena Jacomuzzi, Alice Peroglio Carus, Luca Fuso, Francesca Martra, Piero Sismondi. European Journal of Obstetrics & Gynecology and Reproductive Biology 124 (2006) 232–236.
47. Laparoscopic Systemic Retroperitoneal Lymphadenectomy for Women with Low-Risk Early Endometrial Cancer. Jung Hun Lee, Un Suk Jung, Min Sun Kyung, Jeong-Kyu Hoh, Joong Sub Choi. Ann Acad Med Singapore 2009;38:581-6
48. Laparoscopic Pelvic Surgery for Endometrial Cancer. Eng-Hseon Tay, Ann Acad Med Singapore 2009;38:130-5
49. Comparing Surgical Outcomes in Obese Women Undergoing Laparotomy, laparoscopy, or Laparotomy With Panniculectomy for the Staging of Uterine Malignancy. Eric

L.Eisenhauer, KellyA.Wypych, Babak J.Mehrara, CarrieLawson, Dennis S. Chi, Richard R. Barakat, Nadeem R. Abu-Rustum. Annals of Surgical Oncology 14(8):2384–2391

50. Laparoscopic-Assisted Staging Surgery for Korean Women With Endometrial Cancer. Jung Hun Lee, Un Suk Jung, Min Sun Kyung, Joong Sub Choi. J Society of Lap Surg. (2008)12:150–155
51. Cost and quality-of-life analyses of surgery for early endometrial cancer: laparotomy versus laparoscopy. Spirtos NM, Schlaerth JB, Gross GM, Spirtos TW, Schlaerth AC. Am J Obstet Gynecol 996; 174:1795–800.
52. Laparoscopic assisted vaginal hysterectomy for endometrial cancer. Clinical outcomes and hospital charges. Gemignani ML, Curtin JP, Zelmanovich J, Patel DA, VenKatraman E, Barakat RR. Gynecol Oncol 1999; 73:5-11
53. Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial. Monika Janda, Val Gebski, Alison Brand, Russel Hogg, Thomas W Jobling, Russel Land et al. Contemp Clin Trials. 2006;27:353–63.
54. Incisional bowel herniation after operative laparoscopy: a series of nineteen cases and review of the literature. Boike GM, Miller CE, Spirtos NM, Mercer LJ, Fowler JM, Summit RL, et al. Am J Obstet Gynecol 1995; 172:1726–31.
55. Laparoscopy in endometrial cancer. Javier F. Magrina et al. CME Journal of Gynecologic Oncology 129–131
56. Aalders J, Abeler V, Kolstad P. Recurrent adenocarcinoma of the endometrium: a clinical and histopathological study of 379 patients. Gynecol Oncol 1984;17:85-103.32.

ABSTRACT

Endometrial adenocarcinoma ranks third among gynaecological malignancies after cervix and ovarian cancer in India. The foundation of management of endometrial carcinoma is surgical staging in the form of peritoneal biopsies, omentectomy and pelvic and para aortic lymphadenectomy. The surgical staging is traditionally accomplished by laparotomy but the advent of laparoscopy has made possible this minimally invasive option to be used for achieving the same ends.

A retrospective analysis of all patients who presented with adenocarcinoma of the endometrium and treated surgically at the Cancer Institute (WIA) from the year 2006 to 2010 was done. A total of 145 patients with adenocarcinoma of the endometrium that underwent surgical staging by open or laparoscopic method were analysed. Patient factors like age, BMI and co-morbid illnesses were not significantly different in the two groups. Laparoscopic surgery resulted in significant reduction in hospital stay and incidence of complications especially surgical site infections and paralytic ileus. While it was associated with a significantly prolonged operating time, there was no difference in the median blood loss compared to open surgery. The grade and stage distribution were comparable in the laparotomy and laparoscopy groups and the pelvic nodal yield was equal if not better in the latter group with a trend towards improving nodal yield with the increasing surgical experience of the operating surgeon.

Though long term data was not available, short term results showed that there was no significant difference in the 2-year overall survival and disease free survival between the two groups was there any statistically significant difference in the recurrence rate or disease specific mortality thus proving that laparoscopic approach to surgical staging in carcinoma

endometrium can be performed as safely as the conventional open approach without compromising on the operative, pathological and oncological outcomes.

Key Words: Endometrial adenocarcinoma, surgical staging, laparoscopic hysterectomy, laparoscopic staging, laparoscopic lymphadenectomy, outcomes of laparoscopic staging, complications of laparoscopic staging